Part 3a

Physiology: the cardiovascular system
Intravascular pressure waveforms and the ECG waveform

With the exception of systemic arterial pressure, intravascular pressure waveforms can be observed during pulmonary artery catheterization. An ECG trace is shown on figure 84 to relate the pressure waveforms to the cardiac cycle.

The balloon-tipped catheter is introduced into a central vein and with appropriate scale adjustment the central venous pressure trace, similar to the one opposite, can be seen. The A wave corresponds to atrial contraction, and is followed by the C wave: tricuspid valve closure simultaneous with ventricular contraction. X descent follows, as the right atrium and central vein are now empty and ventricular pressure is now indirectly transmitted across the valve. The right atrium starts filling until the tricuspid valve opens again. The V wave corresponds to the valve opening, following which central venous pressure drops momentarily (the Y descent) as the right atrium empties passively into the right ventricle until the next atrial systole.

The scale is usually adjusted to monitor right ventricular pressures, and the central venous pressure trace is then an undulating waveform around the usual 6–8 mmHg. A straight line indicates a technical problem such as wrong connection or a kinked line.

At 15 cm the balloon is inflated and the catheter advanced downstream. After 20 cm the catheter should enter the right atrium. Right atrial pressure is related to central venous pressure, their difference being the hydrostatic pressure difference; in the supine patient this difference is very small.

Right ventricular pressure trace is instantly recognized when the systolic pressure reaches 20–25 mmHg, while the diastolic pressure should be close to zero.

At about 30 cm, the catheter tip should pass the pulmonary valve and the pulmonary artery pressure trace should be seen. Its shape and amplitude are similar to the ventricular pressure trace; however, the effect of the pulmonary valve closure can be seen as the pressure trace does not return to zero, and the diastolic pressure is about 8–12 mmHg.
Figure 84. ECG waveform and intravascular pressure waveforms
After a further 5–10 cm, the balloon occludes the pulmonary artery and a continuous column of blood should exist between the catheter tip and the left atrium. A pressure trace now recorded is the **pulmonary artery occlusion pressure** (‘wedge pressure’). This corresponds to left atrial pressure and left ventricular filling pressure, provided the following conditions are fulfilled:

- The pulmonary intravascular pressure exceeds extravascular pressure, to obtain a continuous column of blood. This condition is not fulfilled if the intravascular pressure is low, e.g. when the catheter is lodged in West zone 1, or if the extravascular pressure is abnormally high, as with the application of positive end-expiratory pressure.
- The pressure in the left atrium reflects the left ventricular end-diastolic pressure (LVEDP). In mitral valve disease left atrial pressure can be much higher than LVEDP. Conversely, in heart failure when sinus rhythm is preserved, LVEDP may be higher than the mean left atrial pressure: left atrial pressure increases to the high ventricular level only during the atrial systole.

Wedging of the pulmonary artery flotation catheter can be seen on the screen as a sudden decrease in the amplitude of the pressure waveform to < 12 mmHg. (Left heart filling pressure is higher than on the right side.) On deflation of the balloon, a normal pulmonary artery trace should be seen again.

**Arterial pressure waveform** is shown in figure 85 with airway pressure during intermittent positive pressure ventilation. Blood pressure trace shows changes in phase with respiration, called the **respiratory swing**. (For more details of the effects of intermittent positive pressure ventilation on blood pressure see next chapter.) As the intrathoracic pressure is only increased briefly during inspiration, overall effect is a decrease in arterial systolic and diastolic pressure which lags behind the increase in intrathoracic pressure. Respiratory swing is pronounced in hypovolaemia, and is a valuable tool in the estimation of fluid deficit. Notice also that the dicrotic notch is low and the arterial pressure trace is narrow in hypovolaemia. Many ITU monitors have different sweep speeds for arterial pressure and for respiration; association of blood pressure swing and airway pressure is then not observed on the monitor.
Arterial blood pressure and respiratory swing

Figure 85. Arterial blood pressure and respiratory swing
Intermittent positive pressure ventilation causes changes in intrathoracic pressure and blood volume, which are reflected in the cardiovascular parameters. Four phases can be recognized (see figure 86):

- **Phase I**: blood is forced into the left atrium by the increased intrathoracic pressure – blood pressure rises and reflex bradycardia follows.
- **Phase IIa**: blood pressure falls because of decreased venous return – the result of the raised intrathoracic pressure.
- **Phase IIb**: blood pressure is restored to normal by reflex tachycardia.
- **Phase III**: venous return is decreased on lowering the intrathoracic pressure as there is now increased venous capacity in the lungs. Blood pressure falls initially but normalizes soon as reflex tachycardia persists.
- **Phase IV**: persisting tachycardia results in an overshoot of blood pressure; heart rate then drops back to normal (baroreceptor reflex) and blood pressure then also normalizes.

The magnitude of the effect on blood pressure as a result of effects on right and left ventricular filling depends on **blood volume** and the **integrity of the sympathetic nervous system** control, i.e. effects will be exaggerated in the presence of hypovolaemia, sympathetic blockade (this includes general anaesthesia) or autonomic dysfunction (e.g. diabetic neuropathy), or a combination of factors (ill patients, e.g. sepsis), as compensation is lost (‘blocked Valsalva’). The ventilator settings also play a role – fast ventilation rates with a long inspiratory phase will allow little time for compensation; high ventilation pressures will cause greater effects.

In patients with pulmonary hypertension (e.g. severe ARDS), increased airway pressure during intermittent positive pressure ventilation results in increased pulmonary vascular resistance. Interventricular septum may shift to the left and compromise the left ventricular filling, and eventually decrease the stroke volume. Because the lung is leaky in ARDS, inspiration pressure has to be controlled rather than fluids administered to improve left ventricular filling.
Figure 86. Arterial blood pressure and pulse during the Valsalva manoeuvre
SP, DP – systolic and diastolic pressures
P – pulse
Frank–Starling relationship describes the effect of initial fibre length on the force of contraction in the heart muscle. Within physiological limits this relationship is linear (the force of contraction is directly proportional to initial fibre length). Cardiac output is the product of stroke volume and heart rate. Both are under the control of the sympathetic system. In addition, Frank–Starling mechanism ensures that the output (cardiac output) matches the input (preload), by matching the force of contraction to the preload.

The factors which alter venous return (preload) in effect control cardiac output. The most important of these are the following:

- **Venous tone**: any condition associated with sympathetic stimulation will increase cardiac output as a result of reduced venous capacity and increased venous return. The peripheral metabolic need alters the sympathetic tone.
- **Blood volume**: changes in water and salt intake result in temporary changes of blood volume and thus cardiac output. Blood volume and cardiac output are then restored to normal by changes in renal perfusion (and thus changes in urine output). Blood volume expansion is used to compensate for the reduced sympathetic tone under general or regional anaesthesia.
- **Posture**: pooling of blood in dependent parts of the body results in reduced venous return in the upright position – anti-Trendelenburg position also reduces venous return after anaesthesia.

Figures 87–89 show the Frank–Starling relationship under various levels of inotropy and also cardiac work as a product of the force of contraction and fibre length (see chapter on simple mechanics). Only the linear part of the Frank–Starling curve is shown. Cardiac work is the shaded area of the rectangle showing the tension–fibre length relationship during the cardiac cycle. D marks the diastolic fibre length and S the systolic fibre length. Isometric contraction is shown as a rise in tension without a change in length. It can be seen that a heart with a high level of inotropy operates at low pressures and the contraction (from D to S) results in a large difference in length. Compare this with a failing heart, which operates at a high pressure, has a high preload yet contracts poorly – fibre shortening is small, and the bulk of the work is done by a great increase in force. This then perpetuates heart failure. Notice that the shaded area of heart work is roughly the same for all three situations. It can be seen that to improve cardiac function in heart failure, the slope of the Frank–Starling curve has to be increased rather than preload. This is achieved by afterload reduction: the ventricle can eject better, using less force to do the work.
Figure 87. Cardiac work under conditions of high inotropy

Figure 88. Cardiac work in a normal heart

Figure 89. Cardiac work in heart failure
Cardiac cycle: pressure–volume relationships

The filling pressure – end-diastolic volume

The heart fills during the diastole by venous return, augmented, if the heart is in sinus rhythm, by atrial contribution. The pressure–volume relationship in an object being filled is called compliance (dV/dp) – in this case the left ventricular compliance, left ventricular end-diastolic volume and left ventricular end-diastolic pressure. When plotting these quantities graphically (figure 90), the compliance is read as the slope of the volume–pressure relationship: a highly compliant ventricle will have a steep slope, a stiff ventricle a slowly rising one. Note that it is the end-diastolic volume that corresponds to the initial fibre length of the Frank–Starling relationship during systole. For a particular left ventricular compliance, the end-diastolic pressure will increase proportionately with the end-diastolic volume; however, a stiff ventricle will achieve a smaller end-diastolic volume (thus a shorter end-diastolic fibre length) at any given end-diastolic pressure. This has to be borne in mind when interpreting the results of cardiac catheterization: the assumption that left ventricular end-diastolic pressure (estimated from the pulmonary artery occlusion pressure) corresponds to left ventricular end-diastolic volume only applies provided that left ventricular compliance remains unaltered.

Volatile anaesthetics decrease left ventricular compliance to various degrees, and this may be the basis for the extent to which they depress myocardial function.

The left ventricle maintains flow in the systemic circulation. It is a high-pressure system and, therefore, the left ventricle is thick walled.

The right ventricle and pulmonary circulation are a low-pressure system; the filling pressure is about 5 mmHg, and the systolic pressure about 20 mmHg. The ventricle is much more compliant than the left ventricle and thus can match left ventricular output at low pressures.
Figure 90. Left ventricular compliance curves
Generated pressure – stroke volume

During the **isometric phase** of the systole, tension (force) develops in the muscle fibre, which in the next phase relates to the force of contraction. This tension is translated into a sharp rise in ventricular pressure. Ventricular volume during this phase remains essentially constant.

During the **isotonic phase** of systole, cardiac muscle contracts and blood is forced out of the ventricle. Ventricular pressure during this phase remains unaltered; it is the driving pressure for aortic blood flow. During diastole, ventricular pressure rapidly decreases and it remains practically unaltered during the filling.

The **generated pressure–ventricular volume** relationship therefore follows a **loop**, the area of which corresponds to the amount of **cardiac work** – it is the product of pressure and volume (see the chapter on simple mechanics). Ventricular volume corresponds to an extent to the muscle fibre length, and ventricular pressure to the force generated (compare figures 87–89). Figure 91 shows this relationship for different states of contractility. A normal ventricular outflow tract is assumed (the force of contraction is then interchangeable with ventricular pressure). The starting point is ED, the end-diastolic pressure and volume. The isometric and isotonic phases follow in the direction of the arrows to the end-systolic point (ES), and the loop then returns to the end-diastolic point as shown by the arrows. The area of the loop is rectangular and roughly the same for different states of contractility, but its shape differs: a heart that beats effectively achieves a good stroke volume for a modest generated pressure. The failing heart compared with the normal heart does a similar amount of work but less effectively, i.e. it has to develop a greater force and a greater pressure, but ejects less per beat; it also operates at higher pressures. Because of the need for more force to eject, failure is perpetuated. With increased sympathetic drive the heart operates on the steeper cardiac performance curve; less force is needed to do the same amount of work and stroke volume is high for a small amount of generated pressure.
Figure 91. Cardiac work during one cycle as a product of pressure and volume
Following blood loss, the body draws on its reserves to maintain blood flow and oxygen delivery to the tissues. Initially, water is retained by the kidney and extracellular fluid is drawn into the intravascular compartment. If blood loss continues, physiological compensatory mechanisms bring about changes in other physiological parameters to maintain blood flow to the tissues, and in a more severe haemorrhage to the vital organs only. Haemorrhage is classified into four degrees of severity:

- **Class I**: \( \leq 15\% \) or \( \leq 750 \text{ ml blood loss} \). Stroke volume may fall minimally at lower levels of loss, resulting in a minimal tachycardia to maintain cardiac output. This is the situation induced by venesection in a blood donor.
- **Class II**: 15–30\% or 750–1500 ml blood loss. Tachycardia is noticeable while systolic blood pressure is still maintained; diastolic pressure, however, rises due to the higher level of circulating catecholamines. Mean blood pressure is maintained but flow to the organs without autoregulation of blood flow is reduced (e.g. muscle, skin). Because of the reduced skin blood flow, core-to-skin temperature difference starts to rise. Renal blood flow is minimally affected and urine output is maintained at a physiological minimum. Cerebral blood flow is maintained due to autoregulation but anxiety due to the circulating catecholamines is evident.
- **Class III**: 30–40\% or 1500–2000 ml blood loss. The compensatory mechanisms are being exhausted and circulatory failure starts to develop. Tachycardia is marked and there is a measurable fall in systolic blood pressure. Tachypnoea is present due to reduced \( O_2 \) delivery to the tissues. Urine output decreases significantly, core-to-skin temperature difference increases further and mental changes are pronounced.
- **Class IV**: \( \geq 40\% \) or \( \geq 2000 \text{ ml blood loss} \) results in circulatory failure, with compromised blood flow even to vital organs. Tachycardia is very high, systolic blood pressure markedly depressed, while diastolic pressure is still high; thus pulse pressure is very narrow. Urine output is negligible or zero, and if mean pressure falls below the autoregulatory level of the brain, the level of consciousness may be depressed. The skin feels cold because of vasoconstriction. Blood lactate, not shown in figure 91, is significantly increased. Loss of \( \geq 50\% \) or \( \geq 2500 \text{ ml blood loss} \) results in loss of consciousness and total circulatory failure.

Only some measurable physiological parameters are depicted in figure 92; other changes such as skin colour and sweating are important in the evaluation of blood loss.
Figure 92. Changes in physiological parameters with blood loss (classes of haemorrhage)
Normal cerebral blood flow is 54 ml/100g/min (750 ml/min). The formula for flow indicates that flow is given by the ratio of pressure gradient (in this case cerebral perfusion pressure, which is the difference between mean arterial pressure and intracranial pressure), and resistance

\[ Q = \frac{\Delta p}{R} = \frac{\text{MAP} - \text{ICP}}{R}. \]  

(1)

**Autoregulation** exists to maintain, within physiological limits, a constant blood flow to the brain regardless of variations in arterial blood pressure and intracranial pressure; this is done by changes in cerebrovascular resistance, or by changing the perfusion pressure. As shown below, these factors are interrelated.

- **Mean arterial pressure**: Figure 93 shows how autoregulation maintains within physiological limits (normally 60–160 mmHg) constant cerebral blood flow. This is affected by changes in cerebral vascular resistance (see below). In chronic hypertension (or hypotension), the autoregulatory limits are moved up or down respectively. Outside the autoregulatory limits cerebral blood flow is pressure-dependent. When cerebral perfusion pressure is low due to high intracranial pressure (> 25–30 mmHg), baroreceptor stimulation produces systemic hypertension and cardioinhibitory centre stimulation produces reflex bradycardia (Cushing’s reflex).

- **Intracranial pressure**: the relationship between intracranial fluid volume and pressure is shown in figure 94 – cerebral elastance (or ‘stiffness’), defined as \( \frac{\Delta p}{\Delta V} \). Since the intracranial pressure is the dependent variable, it is logical to plot the pressure on the y-axis, and to use the term ‘elastance’ in this context. Elastance is the inverse of cerebral compliance, which is defined as \( \frac{\Delta V}{\Delta p} \). In the graph elastance is given by the slope of the curve at any point, as shown. The skull is a rigid container filled with brain, cerebrospinal fluid and blood. As fluid is essentially incompressible, any increment in cerebral volume (e.g. in cerebral oedema) must be matched by a corresponding decrease of one of the other fluid components; cerebrospinal fluid can be to a certain extent pushed out of the foramen magnum, and venous blood is propelled out as the veins are compressed inside the skull. Since venous blood pressure is one of the components of intracranial pressure, a fall in the former (as venous blood is squeezed out) is accompanied by a fall in the latter. Thus, initially, a small increase in cerebral volume can be accommodated without a significant rise in intracranial pressure. When the compensatory limits are over stretched or lost, any small increment of cerebral volume (e.g. cough, drug or hypercarbia-induced vasodilatation) will be reflected in a steep rise in intracranial pressure, with a detrimental effect on cerebral blood flow.
Figure 93. Cerebrovascular autoregulation

Figure 94. Cerebral elastance curve
Cerebrovascular resistance: the matching of cerebrovascular resistance to cerebral perfusion pressure is the basis of autoregulation of cerebral blood flow. The factors determining cerebrovascular resistance are:

1. **Partial pressure of CO$_2$**: cerebral arteriolar resistance is under the direct influence of local pCO$_2$ across a wide physiological range. Vasodilatation under normal intracranial pressure conditions results in a higher blood flow; this is partly the mechanism of autoregulation: if cerebral blood flow is reduced or if the cerebral metabolic rate is high, cerebral pCO$_2$ rises and pH falls, leading to vasodilatation and restoration of blood flow. In head injury, a mild degree of hypocapnia is preferable when ventilation is controlled under anaesthesia, provided blood pressure is maintained: intracranial pressure will fall as a result of venoconstriction and cerebral blood flow will improve. Very low levels of pCO$_2$ (< 3.4 kPa) lead to symptomatic cerebral ischaemia. Hypercapnia abolishes cerebrovascular autoregulation: cerebral blood flow is then directly proportional to mean arterial blood pressure, (as shown in Figure 95). Conversely, cerebrovascular response to CO$_2$ is blood pressure-dependent: in severe hypotension cerebral blood flow does not change with changes in CO$_2$ tension, as shown in figure 96.

2. **Oxygen partial pressure** in the major cerebral arteries plays a role outside the physiological range; global cerebral blood flow only starts to rise when hypoxia is already significant. At the tissue level, however, O$_2$ partial pressure is probably the mechanism regulating local or regional blood flow in response to hypotension: reduced local blood flow with resulting tissue hypoxia produces immediate arteriolar vasodilatation. High levels of pO$_2$ are associated with a mild degree of vasoconstriction, i.e. reduced cerebral blood flow (as shown in figure 96).

3. **Hydrogen ion concentration**: the effect is similar to, but independent of, pCO$_2$; the hydrogen ion is the mediator of flow metabolism coupling but it is not involved in the response to hypotension.

4. **Blood viscosity** influences vascular resistance as shown in the Hagen–Poiseuille formula (see above). The higher flow in haemodilution compensates (in part only) for otherwise reduced O$_2$ delivery due to the reduced haemoglobin concentration. This mechanism applies in cerebral circulation as in any other part of the body.

5. **Neurogenic and myogenic control**: apart from the humoral factors, the cerebrovascular tone is under sympathetic nervous control, and the autoregulation curve is shifted to the left or right according to the sympathetic tone. Myogenic response (increased tension in response to increased stretch) probably plays a part similar to other parts of the body.

In head injury, autoregulation is lost and the intracranial pressure may be elevated due to the presence of haematoma, cerebral oedema or both. Ventilation may be depressed with resulting hypercapnia: cerebral blood flow is then pressure-dependent. To prevent secondary brain injury, ventilation must be controlled and an adequate O$_2$ delivery to the brain ensured. A cerebral perfusion pressure > 60 mmHg is thought to provide adequate flow. From formula 1 it is then obvious that the desired mean arterial pressure must be kept at a level calculated as the sum of intracranial pressure + 60 mmHg.
Figure 95. Autoregulation of cerebral blood flow within physiological limits; it is abolished by hypercapnia.

Figure 96. Cerebral blood flow as a function of arterial carbon dioxide tension (PaCO₂) and oxygen tension (PaO₂).
Myocardial blood flow is 200 ml/min, or 4% of cardiac output, for an organ weighing only 0.4% of body weight. Oxygen consumption of the heart is also high, 23 ml/min, or 9% of total. This is for a good reason: the heart is a pump that perfuses the rest of the body; its work is hard and it needs a constant energy supply from aerobic metabolism.

The coronary arteries are the first to receive oxygenated blood from the aorta; their **perfusion depends on the pressure gradient generated by the heart**. It is important to remember that coronary arteries run on the epicardial surface. The coronary arterial pressure gradient is thus from epicardium to endocardium, while the intramural pressure gradient during systole is in the opposite direction. Therefore, there is practically no endocardial flow during systole (see figure 97 where coronary artery flow is plotted against the arterial pressure waveform) while the flow in epicardium is maintained. To compensate for the lack of perfusion in systole the subendocardial arteries are thought to be in a chronic state of dilation during diastole. At times of increased demand for perfusion, e.g. tachycardia, hypertension, this region is then unable to increase flow further and thus it is more susceptible to ischaemia.

**Autoregulation**

Unlike the brain, which at times of need receives a higher perfusion pressure via baroreceptor stimulation, the heart cannot effectively increase its oxygen flow by increasing its perfusion pressure since the heart generates the pressure: myocardial oxygen consumption rises proportionately with myocardial work. The heart, therefore, regulates its perfusion only via changes in coronary artery resistance. The oxygen tension in the myocardium or a related parameter is the governing factor. Autoregulation maintains a constant blood flow in the coronary circulation within a wide range of pressures, 60–140 mmHg (see figure 98). It must be kept in mind that the aortic diastolic pressure (not the mean arterial pressure) is the coronary perfusion pressure.

**The sympathetic and parasympathetic nervous system** affects the coronary vascular resistance, but this is modified by autoregulation: α-adrenergic stimulation produces coronary vasoconstriction but if coronary blood flow is compromised autoregulation results in vasodilatation. Parasympathetic stimulation, if unopposed, results in bradycardia. The accompanying fall in oxygen demand produces vasoconstriction; however, if a fast heart rate is maintained, vasodilatation prevails.
Figure 97. Coronary artery flow and arterial blood pressure

Figure 98. Coronary autoregulation
Anaesthetic agents depress myocardial performance and oxygen consumption falls in line with reduced myocardial work (see figure 99). Coronary blood flow therefore is reduced.

Myocardial ischaemia occurs when myocardial oxygen demand exceeds supply, i.e. when coronary blood flow and oxygen flow fall below the minimum required. In a diseased myocardium symptoms of ischaemia occur at a higher perfusion pressure, inside the lower limit of autoregulation. The prediction of cardiac events during anaesthesia is difficult but prevention should be practised: cardiac performance (power) is the product of mean arterial blood pressure and cardiac output. The output is the product of stroke volume and heart rate. Stroke volume is not easily assessed by bedside (or operating tableside) measurements but heart rate and blood pressure are monitored. Thus the rate–pressure product remains a useful clinical tool when estimating myocardial oxygen demand, and therapeutic manoeuvres can be directed at optimizing myocardial performance to maintain oxygen flow to the systemic circulation (which requires adequate cardiac output and haemoglobin concentration) while not overloading the heart by excessive pressures and rates.
Figure 99. Effect of inhalational anaesthesia with halothane on coronary blood flow and myocardial oxygen consumption