Critical care and emergency medicine

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**Cardiovascular signs**
- Cardiac arrest
- Pulse rate <40 or >140 bpm
- Systolic blood pressure (BP) <100 mmHg
- Tissue hypoxia
  - Poor peripheral perfusion
  - Metabolic acidosis
  - Hyperlactataemia
- Poor response to volume resuscitation
- Oliguria: <0.5 ml/kg/hr (check urea, creatinine, K⁺)

**Respiratory signs**
- Threatened or obstructed airway
- Stridor, intercostal recession
- Respiratory arrest
- Respiratory rate < 8 or > 35/min
- Respiratory ‘distress’: use of accessory muscles; unable to speak in complete sentences
- $\text{SpO}_2 < 90\%$ on high-flow $\text{O}_2$
- Rising $\text{PaCO}_2 > 8$ kPa (> 60 mmHg), or > 2 kPa (> 15 mmHg) above ‘normal’ with acidosis

**Neurological signs**
- Threatened or obstructed airway
- Absent gag or cough reflex
- Failure to maintain normal $\text{PaO}_2$ and $\text{PaCO}_2$
- Failure to obey commands
- Glasgow Coma Scale (GCS) < 10
- Sudden fall in level of consciousness (GCS fall > 2 points)
- Repeated or prolonged seizures
A patient with multi-organ failure supported by haemodynamic monitoring, cardiac pacing, a counterpulsation aortic balloon pump, haemofiltration and nitric oxide therapy.
A critically ill patient is one at imminent risk of death; the severity of illness must be recognised early and appropriate measures taken promptly to assess, diagnose and manage the illness.

The approach required in managing the critically ill patient differs from that required in less severely ill patients with immediate resuscitation and stabilisation of the patient’s condition taking precedence:

Priorities are:

- prompt resuscitation, adhering to advanced life support guidelines (p. 556) and the principles of cardiorespiratory management explained in this chapter
- urgent treatment of life-threatening emergencies such as hypotension, hypoxaemia, hyperkalaemia, hypoglycaemia and dysrhythmias
- analysis of the deranged physiology
- establishing the complete diagnosis in stages as further history and the results of investigations become available

ORGANISATION OF CRITICAL CARE

Critical care embraces both intensive care and high-dependency care. Intensive care units (ICUs) are for the care of very ill patients with potential or established organ failure. Initially established for the provision of mechanical ventilation for patients with respiratory failure, ICUs now monitor and support all the major organ systems. High-dependency care provides an intermediate level of care at a point between intensive care and general ward care; it is appropriate both for patients who have had major surgery and for those with single-organ failure. Ideally the ICU should be adjacent to the high-dependency unit (HDU), allowing the critical care medical team to manage a combined critical care department.

The intensive care specialist (intensivist) should provide a holistic approach that coordinates expert opinions from other specialties (surgeons, physicians, microbiologists) to produce an integrated plan of management that recognises the priorities in the treatment of multiple organ failure.

CRITICAL CARE ‘OUTREACH’

Critically ill patients can be found throughout the hospital, in post-operative recovery areas, coronary care units, the acute medical and surgical wards and accident and emergency (A&E) departments. The purpose of ‘outreach’ is to achieve earlier identification of these patients so that assessment and, if appropriate, transfer to ICU/HDU is arranged before deterioration occurs to the point of imminent or actual cardiorespiratory arrest. Prompt identification and treatment may even avert the need for admission to ICU/HDU. Many hospitals are now setting up medical emergency teams or ‘outreach’/’patient at risk’ teams (PARTs). In some hospitals the medical emergency team may be the cardiac arrest team but with a wider remit, while in others this service is provided by the ICU or HDU team.

Criteria that identify deranged physiology (p. 176) are used to alert the ward nursing and junior medical staff to impending problems so that they can summon the outreach team to assess the patient, institute initial resuscitation and supervise transfer to ICU or HDU as appropriate.

ADMISSION GUIDELINES

Rigid rules to determine admission to ICU/HDU are destined to fail because every case must be evaluated on its own merits. Nevertheless, broad guidelines are required to avoid unnecessary suffering and the waste of valuable resources caused by admitting patients who have nothing to gain from intensive care because they either are too well or have no realistic prospect of recovery. The existence of an empty bed does not justify admission. The guiding principle when considering ICU/HDU admission should be the timely use of this resource in patients who have a realistic prospect of recovering to achieve a quality of life that they would value. Patients who do warrant admission should be identified early and admitted without delay since this improves survival and reduces the length of stay on the ICU.

The wishes of the patient, if known, should be respected and whatever decision is made should be carefully explained to the patient’s family.

If the appropriateness of admission remains uncertain, as may occur in the A&E department when little history is available, the patient should be given the benefit of the doubt and the indication for continued active treatment reviewed as further information becomes available (Box 8.1).

There is now evidence that for patients undergoing high-risk elective or emergency surgery the mortality, morbidity and both ICU and hospital length of stay are reduced by pre-operative admission to ICU/HDU to improve cardiorespiratory status (‘pre-optimisation’). Such patients are often elderly with cardiorespiratory disease and poor physiological reserve, and benefit from a protocol of intensive perioperative care. At present many hospitals have major problems in implementing this strategy due to a shortage of critical care beds.

Specific indications for admission to ICU and HDU are given in Box 8.2.

8.1 FACTORS IN THE ASSESSMENT OF A POSSIBLE ICU ADMISSION

- Primary diagnosis and other active medical problems
- Prognosis of underlying condition
- Severity of physiological disturbance—is recovery still possible?
- Life expectancy and anticipated quality of life post-discharge
- Wishes of the patient and/or relatives
- Availability of the required treatment/technology

N.B. Age alone should not be a contraindication to admission.
patients should be accompanied during transfer by an appropriately trained medical escort.

● Patients requiring or likely to require endotracheal intubation and invasive mechanical ventilatory support

● Patients requiring support of two or more organ systems (e.g., inotropes and haemofiltration)

● Patients with chronic impairment of one or more organ systems (e.g., chronic obstructive pulmonary disease (COPD) or severe ischaemic heart disease (IHD)) who also require support for acute reversible failure of another organ system

8.2 ADMISSION CRITERIA FOR ICU AND HDU

Admission to ICU

● Patients requiring or likely to require endotracheal intubation and invasive mechanical ventilatory support

● Patients requiring support of two or more organ systems (e.g., inotropes and haemofiltration)

● Patients with chronic impairment of one or more organ systems (e.g., chronic obstructive pulmonary disease (COPD) or severe ischaemic heart disease (IHD)) who also require support for acute reversible failure of another organ system

Admission to HDU

● Patients who require far more detailed observation or monitoring than can be safely provided on a general ward

   Direct arterial blood pressure (BP) monitoring

   Central venous pressure (CVP) monitoring

   Fluid balance

   Neurological observations, regular Glasgow Coma Scale (GCS) recording

● Patients requiring support for a single failing organ system but excluding invasive ventilatory support

   Mask continuous positive airway pressure (CPAP) or non-invasive (mask) ventilation (NIPPV)—Box 8.17, page 193

   Low- to medium-dose inotropic support

   Renal replacement therapy in an otherwise stable patient

● Patients no longer requiring intensive care but who cannot be safely managed on a general ward

TRANSPORT OF THE CRITICALLY ILL PATIENT

Critically ill patients should be transported to the most appropriate clinical area for their continuing care. Before intra- or inter-hospital transfer is undertaken, the patient’s condition must be stabilised. Appropriate monitoring should be set up and if there is clinical evidence of progressive respiratory failure or inability to protect the airway, endotracheal intubation and ventilation are indicated. Intubation, while often essential, may be hazardous in the critically ill patient with cardiorespiratory failure, and full monitoring and resuscitation facilities must be available. Hypovolaemia and hypotension should be corrected and this will often require monitoring of the central venous pressure (CVP).

Transfer to another hospital may be necessary for further investigations (such as computed tomography, CT), or to specialist liver failure, neurosurgical or cardiac surgical units. The urgency of providing the specialist treatment has to be balanced against the stability of the patient’s condition. It may be more appropriate to admit the patient to the local ICU for initial stabilisation before transfer. All critically ill patients should be accompanied during transfer by an appropriately trained medical escort.

MONITORING

GENERAL PRINCIPLES

On entering an ICU, relatives, students and even clinicians may be intimidated by the numerous tubes and cables attaching each patient to a battery of ‘alarming’ machines (p. 177). Much of the bedside nurse’s time is spent observing, recording and reacting to the information displayed by these monitors, particularly the electrocardiogram (ECG), CVP, arterial blood pressure (BP), temperature and ventilator data. The trends observed over time, interpreted in relation to changes in therapy, are an important guide to the patient’s progress.

The critically ill patient should be monitored according to the following principles:

● Regular clinical examination should never be neglected.

● Simple physical signs such as respiratory rate, the appearance of the patient, restlessness, conscious level and indices of poor peripheral perfusion (pale, cold skin, delayed capillary refill in the nail bed) are just as important as a set of blood gases or numbers impressively displayed on expensive monitors.

● If there is conflict between clinical assessment and the information on a monitor, the monitor should be presumed to be wrong until all potential sources of error have been checked and eliminated. For example, CVP measurement may be erroneous because the line is blocked, the system has not been reset to zero after a change in the patient’s position, the tip of the cannula is lying in the right ventricle, or another infusion has been attached to the same central line.

● Changes and trends are more important than any single measurement.

● Many monitors have alarms which will activate if certain maximum and minimum values are breached. This is a crucial safety feature and may, for example, help to identify the fact that a patient has become disconnected from the ventilator. Despite the understandable desire to avoid extra noise, the alarm limits should always be set to define physiologically ‘safe’ limits for the variable being monitored.

● Sophisticated monitoring systems are often invasive and pose certain hazards, particularly infection (Box 8.3). Always ask ‘Is it necessary?’, and cease monitoring as soon as possible.

MONITORING THE CIRCULATION

Electrocardiogram (ECG)

Standard monitors display a single-lead ECG, record heart rate and identify rhythm changes. More sophisticated machines can print out rhythm strips and monitor ST segment shift, which may be useful in patients with ischaemic heart disease.

Blood pressure

This may be measured intermittently using an automated sphygmomanometer but in critically ill patients continuous intra-arterial monitoring, using a line placed in the radial artery, is preferable. It is important to appreciate that when there is systemic vasoconstriction the mean arterial pressure may be normal or even high although the cardiac output is low. Conversely, if there is peripheral vasodilatation, as in
systolic pressure. A reliable measure of ventricular end-diastolic transmural pressure and causes marked swings in atrial pressures and systemic blood pressure in time with respiration. Pressure measurements should be recorded at end-expiration or, if safe, off the ventilator because these values provide the most reliable measure of ventricular end-diastolic transmural pressure.

Central venous pressure (CVP)

CVP or right atrial pressure (RAP) is monitored using a catheter inserted via either the internal jugular or the subclavian vein with the distal end sited in the upper right atrium. Although on general wards and some HDUs measurements may be made using a saline-filled manometer tube, in ICU the line is transduced as for arterial pressure measurement. The zero reference point used is normally the mid-axillary line (MAL), which approximates to the level of the tricuspid valve or mid-right atrium with the patient lying semi-supine. All intravascular pressures quoted in this chapter are referenced to that point. The classical bedside clinical examination uses the ‘sternal angle’ as the zero reference point and this lies approximately 6–8 cm vertically above MAL. (Values of CVP measured from this reference point will therefore be 6–8 cm lower than values recorded from MAL.)

The CVP is a useful means of assessing the need for intravascular fluid replacement and the rate at which it should be given. If the CVP is low in the presence of a low mean arterial pressure (MAP) or cardiac output, fluid resuscitation is necessary. However, a raised level does not necessarily mean that the patient is adequately resuscitated. It must be remembered that right heart function, pulmonary artery pressure, intrathoracic pressures of both sides of the heart; however, certain conditions such as pulmonary hypertension or right ventricular dysfunction may lead to raised CVP levels even in the presence of hypovolaemia. If this is suspected, it may be appropriate to insert a pulmonary artery flotation catheter (Fig. 8.2) so that pulmonary artery pressure and PAWP, which approximates to left atrial pressure, can be measured. The mean PAWP normally lies between 8 and 12 mmHg (measured from the mid-axillary line) but in left heart failure it may be grossly elevated and even exceed 30 mmHg. Provided the pulmonary capillary membranes are intact, the optimum PAWP when managing acute circulatory failure in the critically ill patient is generally 12–15 mmHg because this will ensure good left ventricular filling without risking hydrostatic pulmonary oedema.

These catheters may also be used to measure cardiac output, sample blood from the pulmonary artery (‘mixed venous’ samples) and, by oximetry, provide continuous monitoring of the mixed venous oxygen saturation ($SvO_2$). Measurement of $SvO_2$ gives an indication of the adequacy of cardiac output in relation to the body’s metabolic requirements and is especially useful in low cardiac output states.

Cardiac output

The most widely used method for cardiac output measurement is the thermodilution technique using a PA catheter. A bolus of cold 5% dextrose is rapidly injected into the right atrium via the CVP line and mixes with the total venous return in the right ventricle, producing a drop in the pulmonary artery temperature that is sensed by a thermistor at the tip of the PA catheter. The cardiac output is derived from the volume and temperature of the injectate and the resulting change in temperature measured in the pulmonary

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In severe hypovolaemia the RAP may be sustained by peripheral vasoconstriction, and transfusion may initially produce little or no change in the CVP (Fig. 8.1).

**Pulmonary artery ‘wedge’ pressure (PAWP) and PA catheterisation**

In most situations the CVP is an adequate guide to the filling pressures of both sides of the heart; however, certain conditions such as pulmonary hypertension or right ventricular dysfunction may lead to raised CVP levels even in the presence of hypovolaemia. If this is suspected, it may be appropriate to insert a pulmonary artery flotation catheter (Fig. 8.2) so that pulmonary artery pressure and PAWP, which approximates to left atrial pressure, can be measured. The mean PAWP normally lies between 8 and 12 mmHg (measured from the mid-axillary line) but in left heart failure it may be grossly elevated and even exceed 30 mmHg. Provided the pulmonary capillary membranes are intact, the optimum PAWP when managing acute circulatory failure in the critically ill patient is generally 12–15 mmHg because this will ensure good left ventricular filling without risking hydrostatic pulmonary oedema.

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artery; it is inversely related to the area under the temperature–time curve. Although generally viewed as the ‘gold standard’ for clinical measurement of cardiac output, the error may be 10–15%.

Thermodilution cardiac output measurement has been refined by the development of PA catheters incorporating a heating element, which raises blood temperature at frequent intervals, with the resultant temperature change also detected by the thermistor. These ‘continuous’ cardiac output catheters dispense with the need for injections of cold dextrose.

Increasingly less invasive methods for monitoring cardiac output are being used, such as oesophageal Doppler ultrasonography. This involves inserting a 6 mm probe into the distal oesophagus to allow continuous monitoring of the aortic flow signal from the descending aorta (Fig. 8.3). From the stroke distance (area under velocity/time waveform), and using a correction factor that incorporates the patient’s age, height and weight, an estimate of left ventricular stroke volume and hence cardiac output can be made. Peak velocity is an indicator of left ventricular performance while flow time is an indicator of left ventricular filling and peripheral resistance. Oesophageal Doppler provides a rapid and clinically useful assessment of volume status and cardiac performance to guide early fluid and vasoactive therapy.

Analysis of arterial pressure waveform is another means of continuously estimating cardiac output, and can be calibrated either by transpulmonary thermodilution (PiCCO) or lithium dilution methods (LidCO).

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**Urine output**

This is a sensitive measure of renal perfusion, provided that the kidneys are not damaged (e.g. acute tubular necrosis) or affected by drugs (e.g. diuretics, dopamine), and can be monitored accurately if a urinary catheter is in place. It is
normally measured hourly and the lower limit of normal is 0.5 ml/hr/kg body weight.

**Fluid balance**
Assessing fluid balance in critically ill patients is a difficult but important discipline. Weighing the patient daily can be helpful but is extremely difficult, and assessment is usually based on fluid balance charts which record:
- inputs: oral, nasogastric and intravenous, classified as crystalloid and colloid
- outputs: urine, nasogastric, fistulae, vomiting, diarrhoea and surgical drain losses.

The insensible loss from skin, respiration etc. is normally 500–1000 ml/day but can exceed 2 litres/day in a pyrexial patient with open wounds.

**Peripheral/skin temperature**
This is conventionally measured over the dorsum of the foot and reflects cutaneous blood flow and venous filling. The gradient between peripheral and central or ‘core’ temperature (from rectal, oesophageal or tympanic probes) may be used to assess peripheral perfusion; a difference of < 3°C suggests that both intravascular fluid replacement and tissue perfusion are adequate.

**Blood lactate, hydrogen ion and base deficit**
A metabolic acidosis with base deficit > 5 mmol/l requires explanation (p. 437). It often indicates increased lactic acid production in poorly perfused, hypoxic tissues and impaired lactate metabolism due to poor hepatic perfusion. Serial lactate measurements may therefore be helpful in monitoring tissue perfusion and the response to treatment. Other conditions such as acute renal failure, ketoacidosis and poisoning may be the cause (p. 438). Large volume infusions of fluids containing sodium chloride, e.g. in theatre or during resuscitation, may lead to a hyperchloraemic acidosis.

**Arterial blood gases**
These are usually measured several times a day in a ventilated patient so that inspired oxygen (\( F_{\text{I}O_2} \)) and minute volume can be adjusted to achieve the desired \( Pa_{O_2} \) and \( Pe_{CO_2} \) respectively. Analysis of arterial blood gas results is also a useful means of monitoring disturbances of acid–base balance (Ch. 16).

**Lung function**
In ventilated patients lung function is monitored by:
- alveolar–arterial \( PO_2 \) gradient and hypoxaemia index (\( Pa_{O_2}/Fi_{O_2} \)), both measures of gas exchange
- arterial and end-tidal \( CO_2 \), reflecting alveolar ventilation
- tidal volume (\( V_T \)), respiratory rate (\( f \)), minute volume (\( V_T \times f \)), airway pressure and compliance, reflecting airways resistance, the ‘stiffness’ of the lungs and the ease with which the patient can meet the required work of breathing.

**Capnography**
The \( CO_2 \) concentration in inspired gas is zero, but during expiration, after clearing the physiological dead space, it rises progressively to reach a plateau which represents the alveolar or end-tidal \( CO_2 \) concentration. This cyclical change in \( CO_2 \) concentration or capnogram is measured using an infrared sensor inserted between the ventilator tubing and the endotracheal tube. With normal lungs, the end-tidal \( CO_2 \) closely mirrors \( Pa_{CO_2} \) and can be used to assess the adequacy of alveolar ventilation. However, there may be considerable discrepancies if there is lung disease or impaired pulmonary perfusion (for example, due to hypovolaemia). Trends in end-tidal \( CO_2 \) are useful in head injury management and during the transport of ventilated patients.

In combination with the gas flow and respiratory cycle data from the ventilator, \( CO_2 \) production and hence metabolic rate may be calculated.

**MONITORING RESPIRATORY FUNCTION**

**Oxygen saturation (\( SpO_2 \))**
This is measured by a probe, usually attached to a finger or earlobe. Spectrophotometric analysis is used to determine the relative proportions of saturated and desaturated haemoglobin. The technique is unreliable if peripheral perfusion is poor and may produce erroneous results in the presence of nail polish, excessive movement or high ambient light. In general, arterial oxygenation is satisfactory if \( SpO_2 \) is greater than 90%. In the ICU, sudden falls in \( SpO_2 \) may be caused by:
- pneumothorax
- displacement of the endotracheal tube
- disconnection from the ventilator
- lung collapse due to thick secretions blocking the proximal bronchial tree
- circulatory collapse causing a poor signal due to impaired peripheral perfusion
- error such as a detached probe.

**PHYSIOLOGY OF THE CRITICALLY ILL PATIENT**

**OXYGEN TRANSPORT**
The major function of the heart, lungs and circulation is the provision of oxygen and other nutrients to the various organs and tissues of the body. During this process carbon dioxide and the other waste products of metabolism are removed. The rate of supply and removal should match the specific metabolic requirements of the individual tissues. This requires adequate oxygen uptake in the lungs, global matching of delivery and consumption, and regional control of the circulation. Failure to supply sufficient oxygen to meet the metabolic requirements of the tissues is the cardinal feature of circulatory failure or ‘shock’.

The transport of oxygen from the atmosphere to the mitochondria within individual cells is illustrated in Figure 8.4. The important points to note are that:
The movement of oxygen from pulmonary capillary to systemic tissue capillary, referred to as the global oxygen delivery (DO₂), relies on convection or bulk flow and is the product of cardiac output and arterial oxygen content.

The regional distribution of oxygen delivery is vital. If skin and muscle receive high blood flows but the splanchnic bed does not, the gut will become hypoxic even if overall oxygen delivery is high.

The major determinants of the oxygen content of arterial blood (CaO₂) are the arterial oxygen saturation of haemoglobin (SaO₂) and the haemoglobin concentration (over 95% of oxygen carried in the blood is attached to haemoglobin). The shape of the oxyhaemoglobin dissociation curve dictates that increases in PaO₂ beyond the level that ensures SaO₂ is > 90% produce relatively small additional increases in CaO₂ (Fig. 8.5). Consider a patient who is both anaemic (Hb 60 g/l) and hypoxaemic (SaO₂ 75%) when breathing air (FiO₂ 0.21). Supplementary oxygen at FiO₂ 0.4 will increase SaO₂ to 93%; CaO₂ will increase by 24% but further increases in FiO₂ while increasing PaO₂ cannot produce any further useful increases in SaO₂ or CaO₂. However, increasing Hb to 90 g/l by blood transfusion will result in a further 50% increase in CaO₂.

The movement of oxygen from tissue capillary to cell occurs by diffusion and depends on the gradient of oxygen partial pressures, diffusion distance and the ability of the cell to take up and use oxygen. Therefore microcirculatory, tissue diffusion and cellular factors, as well as DO₂, influence the oxygen status of the cell.

Supranormal levels of oxygen delivery cannot compensate for diffusion problems between capillary and cell, nor for metabolic failure within the cell.
2,3 diphosphoglycerate (DPG). are defined by the position and the effect of various physico-chemical factors. The dotted line illustrates the rightward shift of the curve (i.e. $P_d$ increases) caused by increases in temperature, $PaCO_2$, metabolic acidosis and 2,3 diphosphoglycerate (DPG).

**OXYHAEMOGLOBIN DISSOCIATION CURVE**

The oxyhaemoglobin dissociation curve (Fig. 8.5) describes the relationship between the saturation of haemoglobin ($SO_2$) and the partial pressure ($PO_2$) of oxygen in the blood. Due to the shape of the curve, a small drop in $PO_2$ below 8 kPa (60 mmHg) will cause a marked fall in $SO_2$. Its position and the effect of various physico-chemical factors are defined by the $PO_2$ at which 50% of the haemoglobin is saturated ($P_{50}$), which is normally 3.5 kPa (26 mmHg).

A shift in the curve will influence the uptake and release of oxygen by the Hb molecule; for example, if the curve moves to the right, the haemoglobin saturation will be lower for any given oxygen tension and therefore less oxygen will be taken up in the lungs but more will be released to the tissues. As capillary $PCO_2$ rises, the curve moves to the right, increasing unloading of oxygen in the tissues—a phenomenon known as the Bohr effect.

Traditionally, the optimum haemoglobin concentration for critically ill patients had been considered to be approximately 100 g/l, representing a balance between maximising the oxygen content of the blood and avoiding regional microcirculatory problems due to increased viscosity. However, recent evidence suggests an improved outcome in critically ill patients if the haemoglobin concentration is maintained between 70 and 90 g/l, with the exception of the elderly and patients with coronary artery disease, in whom a level of 100 g/l remains appropriate.

**OXYGEN CONSUMPTION**

The sum of the oxygen consumed by the various organs represents the global oxygen consumption ($VO_2$) and is approximately 250 ml/min for an adult of 70 kg undertaking normal daily activities. $VO_2$ may be calculated indirectly from the product of cardiac output and the arterial mixed venous oxygen content difference ($CaO_2$-$CvO_2$), as shown in Figure 8.4, or directly by sampling the inspired and mixed-expired gases from the ventilator and measuring inspired and expired minute volume using either a mass spectrometer or metabolic cart.

The oxygen saturation in the pulmonary artery, otherwise known as the mixed venous oxygen saturation ($SvO_2$), represents a measure of the oxygen not consumed by the tissues ($DO_2$-$VO_2$). The saturation of venous blood from different organs varies considerably; for example, the hepatic venous saturation usually does not exceed 60% but the renal venous saturation may reach 90%, reflecting the great difference in both the metabolic requirements of these organs and the oxygen content of the blood delivered to them. $SvO_2$ is influenced by changes both in oxygen delivery ($DO_2$) and consumption ($VO_2$) and, provided the microcirculation and the mechanisms for cellular oxygen uptake are intact, can be used to monitor whether global oxygen delivery is adequate to meet overall demand.

The reoxygenation of the blood that returns to the lungs and the resulting arterial saturation ($SaO_2$) will depend on how closely pulmonary ventilation and perfusion are matched. If part of the pulmonary blood flow perfuses non-ventilated parts of the lung, there will be ‘shunting’, and the blood entering the left atrium will be desaturated in proportion to the size of this shunt and the level of $SvO_2$.

**RELATIONSHIP BETWEEN OXYGEN CONSUMPTION AND DELIVERY**

The tissue oxygen extraction ratio (OER), which is 20–25% in a normal subject at rest, rises as consumption increases or supply diminishes (Fig. 8.6). The maximum OER is approximately 60% for most tissues; at this point no further increase in extraction can occur and any further increase in oxygen consumption or decline in oxygen delivery will cause tissue hypoxia, anaerobic metabolism and increased lactic acid production.

In sepsis the slope of maximum OER decreases, reflecting the reduced ability of tissues to extract oxygen (DE cf. AB on Fig. 8.6), but the curve does not plateau and oxygen consumption continues to increase even at ‘supranormal’ levels of oxygen delivery. This concept encouraged some physicians to treat septic shock using vigorous intravenous fluid loading and inotropic support, usually with dobutamine, with the aim of achieving very high oxygen deliveries (> 600 ml/min/m²) in the belief that this strategy would increase oxygen consumption, relieve tissue hypoxia, prevent multiple organ failure and improve prognosis. Trials have demonstrated no benefit in ICU patients with established organ failure but suggest that it may be worthwhile if applied before organ failure supervenes (Box 8.4).
The mediators and clinical manifestations of the inflammatory response are described on pages 75–76. In critically ill patients these processes have important consequences (Box 8.5).

Fever, tachycardia with warm peripheries, tachypnoea and a raised white cell count traditionally prompt a diagnosis of sepsis with the implication that the clinical picture is caused by invading microorganisms and their breakdown products. However, other conditions such as pancreatitis, trauma, cardiopulmonary bypass, vasculitis etc. can also produce the same clinical picture in the absence of infection.

Local inflammation
The body’s initial response to a noxious local insult is to produce a local inflammatory response with sequestration and activation of white blood cells and the release of a variety of mediators to deal with the primary ‘insult’ and prevent further damage either locally or in distant organs.

Normally, a delicate balance is achieved between pro- and anti-inflammatory mediators. However, if the inflammatory response is excessive, local control is lost and a large array of mediators including prostaglandins, leukotrienes, free oxygen radicals and particularly pro-inflammatory cytokines (p. 66) are released into the circulation.

The inflammatory and coagulation cascades are intimately related. The process of blood clotting not only involves platelet activation and fibrin deposition but also causes activation of leucocytes and endothelial cells. Conversely, leucocyte activation induces tissue factor expression and initiates coagulation. Control of the coagulation cascade is achieved through the natural anti-coagulants antithrombin (AT) III, activated protein C (APC) and tissue factor pathway inhibitor (TFPI) which not only regulate the initiation and amplification of the coagulation cascade but also inhibit the pro-inflammatory cytokines. Deficiency of ATIII and APC (features of disseminated intravascular coagulation (DIC), see below) facilitates thrombin generation and promotes further endothelial cell dysfunction.

Systemic inflammation
During a severe inflammatory response systemic release of cytokines and other mediators triggers widespread interaction between the coagulation pathways, platelets, endothelial cells and white blood cells, particularly the polymorphonuclear cells (PMNs). These ‘activated’ PMNs...
express adhesion factors (selectins) causing them initially to adhere to and roll along the endothelium, then to adhere firmly and finally to migrate through the damaged and disrupted endothelium into the extravascular, interstitial space together with fluid and proteins, resulting in tissue oedema and inflammation. A vicious circle of endothelial injury, intravascular coagulation, microvascular occlusion, tissue damage and further release of inflammatory mediators ensues.

All organs may become involved. This manifests in the lungs as the acute respiratory distress syndrome (ARDS) and in the kidneys as acute tubular necrosis (ATN), while widespread disruption of the coagulation system results in the clinical picture of DIC.

The endothelium itself produces mediators that locally control blood vessel tone: endothelin 1, a potent vasoconstrictor, and prostacyclin and nitric oxide (NO, p. 76) which are systemic vasodilators. NO (which is also generated outside the endothelium) is implicated in both the myocardial depression and the profoundly vasodilated circulation (both arterioles and venules) that causes the relative hypovolaemia and systemic hypotension found in septic/SIRS shock.

If both the precipitating cause and accompanying circulatory failure (hypotension and frequently severe hypovolaemia due to venodilatation and fluid loss through the leaky vascular endothelium) are promptly controlled before significant organ failure occurs ('early' shock), the prognosis is good. However, if the global and peripheral circulatory failure is not corrected promptly, and particularly if the underlying cause is not effectively treated, progressive deterioration in organ function occurs and multiple organ failure (MOF) ensues ('late' shock).

The mortality of MOF is high and increases with the number of organs that have failed, the duration of organ failure and the patient’s age. Failure of four or more organs is associated with a mortality > 80%.

### 8.6 TYPICAL CIRCULATORY MEASUREMENTS IN A NORMAL ADULT AND IN VARIOUS CARDIORESPIRATORY CONDITIONS THAT MAY CAUSE CIRCULATORY ‘SHOCK’

<table>
<thead>
<tr>
<th>Clinical condition</th>
<th>RAP/CVP (mmHg)</th>
<th>LAP/PAPWP (mmHg)</th>
<th>PAP (mmHg)</th>
<th>MAP (mmHg)</th>
<th>Heart rate (b/min)</th>
<th>Cardiac output (l/min)</th>
<th>SVR*</th>
<th>PVR*</th>
<th>CaO₂ (ml/l)</th>
<th>DO₂ (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>6</td>
<td>11</td>
<td>16</td>
<td>96</td>
<td>70</td>
<td>5</td>
<td>18</td>
<td>1</td>
<td>200</td>
<td>1000</td>
</tr>
<tr>
<td>Major haemorrhage</td>
<td>0</td>
<td>4</td>
<td>11</td>
<td>81</td>
<td>120</td>
<td>3</td>
<td>27</td>
<td>2.3</td>
<td>160</td>
<td>480</td>
</tr>
<tr>
<td>Left heart failure</td>
<td>8</td>
<td>20</td>
<td>24</td>
<td>96</td>
<td>100</td>
<td>3.7</td>
<td>24</td>
<td>1</td>
<td>180</td>
<td>670</td>
</tr>
<tr>
<td>Major pulmonary embolism</td>
<td>12</td>
<td>6</td>
<td>36</td>
<td>81</td>
<td>110</td>
<td>2.5</td>
<td>28</td>
<td>12</td>
<td>160</td>
<td>400</td>
</tr>
<tr>
<td>Exacerbation of COPD</td>
<td>11</td>
<td>10</td>
<td>42</td>
<td>82</td>
<td>100</td>
<td>6</td>
<td>12</td>
<td>5</td>
<td>150</td>
<td>900</td>
</tr>
<tr>
<td>Septic shock</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-volume load</td>
<td>3</td>
<td>8</td>
<td>16</td>
<td>55</td>
<td>130</td>
<td>4.5</td>
<td>12</td>
<td>1.3</td>
<td>150</td>
<td>675</td>
</tr>
<tr>
<td>Post-volume load</td>
<td>9</td>
<td>15</td>
<td>23</td>
<td>60</td>
<td>120</td>
<td>7.5</td>
<td>7</td>
<td>1.1</td>
<td>140</td>
<td>1050</td>
</tr>
</tbody>
</table>

* Multiply by 80 to give SI units: dyn.sec/cm². To adjust for the size of the patient, the measurements of flow and resistance are frequently indexed by dividing by the patient’s body surface area.

(RAP/LAP = right/left atrial pressure; CVP = central venous pressure; PAWP = pulmonary artery wedge pressure; PAP/MAP = pulmonary artery/mean arterial pressure; SVR/PVR = systemic/pulmonary vascular resistance; CaO₂ = arterial oxygen content; DO₂ = global oxygen delivery; COPD = chronic obstructive pulmonary disease)

**Note** These values are merely examples. The severity of the condition and pre-existing cardiopulmonary disease will affect the precise figures obtained in individual cases. Note that in contrast to other conditions the oxygen delivery is high in septic shock after volume loading. When the circulatory abnormalities have been defined in this way, appropriate management may be planned.

Pressures quoted referenced to zero at mid-axilla as is usual practice in ICU. Subtract vertical distance from mid-axilla to sternal angle (approx. 6–8 mmHg) if sternal angle used as reference point.
The many causes of circulatory failure or ‘shock’ may broadly be classified into:

- **hypovolaemic**—any condition provoking a major reduction in blood volume, e.g. internal or external haemorrhage, severe burns, dehydration
- **cardiogenic**—any form of severe heart failure, e.g. myocardial infarction, acute mitral regurgitation
- **obstructive**—obstruction to blood flow around the circulation, e.g. major pulmonary embolism, cardiac tamponade, tension pneumothorax
- **neurogenic**—caused by major brain or spinal injury producing disruption of brain stem and neurogenic vasomotor control; may be associated with neurogenic pulmonary oedema
- **anaphylactic**—inappropriate vasodilatation triggered by an allergen (e.g. bee sting)
- **septic/SIRS**—infection or other causes of a systemic inflammatory response that produce widespread endothelial damage with vasodilatation, arteriovenous shunting, microvascular occlusion and tissue oedema, resulting in organ failure.

### Clinical assessment and complications

Although dependent to some extent on the underlying cause, a range of clinical features are common to most cases (Box 8.7 and p. 177).

Hypovolaemic, cardiogenic and obstructive causes of circulatory failure produce the ‘classical’ image of shock, with cold peripheries, weak central pulses and evidence of a low cardiac output. In contrast, neurogenic, anaphylactic and septic shock are usually associated with warm peripheries, bounding pulses and features of a high cardiac output. The central venous pressure (jugular venous pressure, JVP) is typically reduced in hypovolaemic and anaphylactic shock but elevated in cardiogenic and obstructive shock, and may be low, normal or high in neurogenic and septic shock. This is an important distinction and direct measurement of the CVP or PAWP (Fig. 8.2, p. 181) may be very helpful if the physical signs are difficult to interpret. Figure 8.7 indicates how the likely diagnosis may be established by careful analysis of the CVP, peripheral perfusion, pulse volume and haematocrit. All forms of shock require early identification and treatment because, if inadequate regional tissue perfusion and cellular dysoxia persist, multiple organ failure will develop.

### RESPIRATORY FAILURE INCLUDING ARDS

The majority of patients admitted to ICU/HDU will have respiratory problems either as the primary cause of their admission or secondary to pathology elsewhere. Respiratory failure is formally classified on the basis of blood gas analysis into:

![Fig. 8.7 A guide to the initial analysis and diagnosis of circulatory shock.](image-url)
● type 1—hypoxaemia ($PaO_2 < 8$ kPa (< 60 mmHg) when breathing air) without hypercapnia caused by a failure of gas exchange due to mismatching of pulmonary ventilation and perfusion
● type 2—hypoxaemia with hypercapnia ($PaCO_2 > 6.5$ kPa (> 49 mmHg)) due to alveolar hypoventilation which occurs when the respiratory muscles cannot perform sufficient effective work to clear the carbon dioxide produced by the body.

Although this distinction is conceptually useful, it cannot be applied too rigidly in critically ill patients since they may change from type 1 to 2 as their illness progresses. For example, hypercapnia may develop in pneumonia or pulmonary oedema as the patient tires and can no longer sustain the increased work of breathing.

Pulmonary problems in critically ill patients can also be classified according to the functional residual capacity (FRC, or the lung volume at the end of expiration). Examples of low FRC include lung collapse, pneumonia and pulmonary oedema; examples of a high FRC (i.e. over-distended lungs) include asthma, COPD and bronchiolitis. This allows logical management directed at improving lung compliance and reducing the work of breathing.

The more common causes of acute respiratory failure presenting to ICU/HDU for respiratory support are shown in Box 8.8.

The presentation, differential diagnosis and initial treatment of the primary respiratory conditions causing acute respiratory failure are covered in Chapter 19.

The assessment of respiratory failure in the critically ill patient should be guided by several important principles:

● The patient’s appearance (tachypnoea, difficulty speaking in complete sentences, laboured breathing, exhaustion, agitation or increasing obtundation) is more important than measurement of blood gases in deciding when it is appropriate to provide mechanical respiratory support or intubation.

● Adequate supplemental oxygen to maintain $SpO_2 > 94\%$ should be provided. If the inspired oxygen concentration required exceeds 0.6, refer to the critical care team.

● Monitoring of $SpO_2$ and arterial blood gases is helpful in documenting progress.

● Restless patients dependent on supplementary oxygen or with deteriorating conscious level are at risk. If they remove the mask or vomit, the resulting hypoxaemia or aspiration may be catastrophic.

● An attempt should be made to reduce the work of breathing, e.g. by treating bronchoconstriction or using CPAP (Box 8.17, p. 193).

**ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)**

This describes the acute, diffuse pulmonary inflammatory response to either direct (via airway or chest trauma) or indirect blood-borne insults that originate from extra-pulmonary pathology. It is characterised by neutrophil sequestration in pulmonary capillaries, increased capillary permeability, protein-rich pulmonary oedema with hyaline membrane formation, damage to type 2 pneumocytes leading to surfactant depletion, alveolar collapse and reduction in lung compliance. If this early phase does not resolve with treatment of the underlying cause, a fibroproliferative phase ensues and causes progressive pulmonary fibrosis. It is frequently associated with other organ dysfunction (kidney, heart, gut, liver, coagulation) as part of multiple organ failure. The term ARDS is often limited to patients requiring ventilatory support on the ICU, but less severe forms, conventionally referred to as acute lung injury (ALI) and with similar pathology, occur on acute medical and surgical wards. The clinical symptoms and

---

### 8.8 COMMON CAUSES OF RESPIRATORY FAILURE IN CRITICALLY ILL PATIENTS

<table>
<thead>
<tr>
<th>Type 1 respiratory failure</th>
<th>Type 2 respiratory failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>Reduced respiratory drive,*</td>
</tr>
<tr>
<td>Pulmonary oedema*</td>
<td>e.g. drug overdose, head injury</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>Upper airway obstruction (oedema, infection, foreign body)</td>
</tr>
<tr>
<td>Pulmonary fibrosis</td>
<td>Late severe acute asthma</td>
</tr>
<tr>
<td>ARDS*</td>
<td>COPD</td>
</tr>
<tr>
<td>Aspiration</td>
<td>Peripheral neuromuscular disease, e.g. Guillain–Barré, myasthenia gravis</td>
</tr>
<tr>
<td></td>
<td>Flail chest injury</td>
</tr>
<tr>
<td></td>
<td>Exhaustion* (includes all type 1 causes)</td>
</tr>
</tbody>
</table>

* Secondary complications of other diseases.

---

Fig. 8.8 Chest X-ray in acute respiratory distress syndrome (ARDS). This 22-year-old woman was involved in a road traffic accident. Note bilateral lung infiltrates, pneumomediastinum, pneumothoraces with bilateral chest drains, surgical emphysema, and fractures of the ribs, right clavicle and left scapula.
signs are not specific, sharing many features with other pulmonary conditions. The criteria defining ARDS are:

- hypoxaemia, defined as $FIO_2/PaO_2 < 26.7 \text{ kPa (} < 200 \text{ mmHg)}$
- chest X-ray showing diffuse bilateral infiltrates (Fig. 8.8)
- absence of a raised left atrial pressure: PAWP < 15 mmHg
- impaired lung compliance.

The term ARDS has severe limitations as a diagnostic label since, like jaundice or a raised CVP, it represents a response to a variety of primary conditions (Box 8.9).

## RENAL FAILURE

Oliguria is frequently an early sign of systemic problems in critical illness and successful resuscitation is associated with restoration of good urine output, an improving acid–base balance and correction of plasma potassium, urea and creatinine. Acute renal failure (p. 481) in the context of critical illness is usually due to pre-renal factors such as uncorrected hypovolaemia, hypotension or ischaemia causing acute tubular necrosis (ATN). Sepsis is frequently a compounding factor, causing both global hypotension and local ischaemia that is often associated with DIC. In the presence of pre-existing chronic renal impairment or nephotoxic drugs, acute renal failure may result from relatively minor ischaemic or hypotensive insults. While ATN is by far the most common cause of acute renal failure in the ICU, it is essential not to overlook other causes, such as renal tract obstruction (including a blocked urinary catheter), drug toxicity, acute glomerulonephritis and vasculitis associated with connective tissue diseases such as systemic lupus erythematosus. Appropriate investigations such as urinary microscopy, immunopathological tests and abdominal ultrasound to exclude renal tract obstruction need to be carried out at an early stage.

## NEUROLOGICAL FAILURE (COMA)

Impaired consciousness or coma is often an early feature of severe systemic illness (Box 8.10). Prompt assessment of conscious level and management of airway, breathing and circulation are essential to prevent further brain injury, to allow diagnosis and for definitive treatment to be instituted.

Impairment of conscious level is objectively graded according to the Glasgow Coma Scale (GCS, p. 1186), which is also used to monitor progress. Although necessarily limited, careful neurological examination is very important in the unconscious patient. Pupil size and reaction to light, presence or absence of neck stiffness, focal neurological signs and evidence of other organ impairment should be noted. After cardiorespiratory stability is achieved, the cause of the coma must be sought from history (family, witness, general practitioner), examination and investigation, particularly CT. The possibility of drug overdose should always be considered. The direct neurological causes of coma are listed and described in Chapter 26.

## SEPSIS

Any or all of the features of SIRS (Box 8.5, p. 185) may be present, together with an obvious focus of infection such as purulent sputum from the chest with shadowing on chest X-ray or erythema around an intravenous line. However, severe sepsis may present as unexplained hypotension (i.e. septic shock) and the speed of onset may simulate a major pulmonary embolus or myocardial infarction. The common sites of infection in critically ill patients and some of the appropriate investigations to consider are listed in Box 8.11.

The patient may be admitted with infection from home (‘community-acquired’) or may develop it after admission to the unit (‘nosocomial’). The likely causative microorganism and the antibiotic sensitivities will depend on this important distinction, which therefore directs the initial choice of antibiotics. Initial investigations should include:

- cultures of blood, sputum, intravascular lines, urine and any wound discharges
- coagulation profile, plasma lactate, arterial blood gases, urinalysis and chest X-ray.

As few as 10% of ICU patients with a clinical diagnosis of ‘septic’ shock will have positive blood cultures, due to the effects of prior antibiotic treatment and the fact that a patient with an inflammatory state is not necessarily infected.
Specific investigations will be driven by the history and examination. For example, erect/decubitus abdominal X-rays, ultrasound and CT might be considered in cases of suspected intra-abdominal sepsis (Box 8.11).

The most important objective in management is to identify and treat the underlying cause. Nosocomial infections are an increasing problem on critical care units (Box 8.12). Cross-infection is a major concern, particularly with regard to meticillin-resistant Staphylococcus aureus (MRSA) and multidrug-resistant Gram-negative organisms, and if this is frequent it should prompt a review of the unit’s infection control policies. The most important practice in preventing cross-infection is thorough hand-washing after every patient contact. Limiting the use of antibiotics helps to prevent the emergence of multidrug-resistant bacteria.

**DISSEMINATED INTRAVASCULAR COAGULATION (DIC)**

This is also known as consumptive coagulopathy and is one of the acquired disorders of haemostasis (p. 1060); it is common in critically ill patients and often heralds the onset of multi-organ failure. The condition is characterised by an increase in prothrombin time, partial thromboplastin time and fibrin degradation products, and a fall in platelets and fibrinogen. The clinically dominant feature may be widespread bleeding from vascular access points, gastrointestinal tract, bronchial tree and surgical wound sites, or widespread microvascular and even macrovascular thrombosis. Management is supportive with infusions of fresh frozen plasma and platelets while the underlying cause is treated.

**GENERAL PRINCIPLES OF CRITICAL CARE MANAGEMENT**

Critically ill patients should be assessed regularly and at least twice daily on morning and evening ward rounds. Initially, it seems daunting to perform such an assessment,
MANAGEMENT OF MAJOR ORGAN FAILURE

CIRCULATORY SUPPORT

The primary goals (Box 8.14) are to:

● Restore global oxygen delivery (DO₂) by ensuring adequate cardiac output.
● Maintain an MAP that ensures adequate perfusion of vital organs. The target will be patient-specific depending on pre-morbid factors (e.g., hypertension or coronary artery disease) and may range from 60 to 80 mmHg.
● Avoid levels of left atrial pressure that produce pulmonary oedema and compromise gas exchange. This may limit the degree of volume resuscitation in the presence of acute lung injury/ARDS.

The first objective is to ensure that an ‘appropriate’ ventricular preload is restored. Vasoactive drugs should not be used as a substitute for adequate volume resuscitation.

The key determinants of DO₂ and MAP are cardiac output and arteriolar resistance which are in turn determined by the ventricular ‘preload’, ‘afterload’, myocardial contractility and heart rate.

PRELOAD

The atrial filling pressures (RAP or CVP, LAP or PAWP) or preload determine the end-diastolic ventricular volume which, according to Starling’s Law and depending on the myocardial contractility, defines the force of the next cardiac contraction (Fig. 8.21, p. 543). The predominant factor influencing preload is venous return, which is determined by the intravascular volume and the venous ‘tone’ (Box 8.15).

When volume is lost (e.g., major haemorrhage), venous ‘tone’ increases and this helps to offset the consequent fall in atrial filling pressure and cardiac output. If the equivalent volume is returned gradually, the right atrial pressure will return to normal as the intravascular volume is restored and the reflex increase in venous tone abates. However, if fluid is infused too rapidly there will be insufficient time for the venous and arteriolar tone to fall and pulmonary oedema may occur, even though the intravascular volume has only been restored to the pre-morbid level.

If the preload is low, volume loading with intravenous fluids is the priority and the most appropriate means of improving cardiac output and oxygen delivery. The choice of fluid for volume loading is controversial. No clear advantage of colloid over crystalloid has ever been demonstrated, but adequate filling is achieved with smaller volumes of colloid. Red cells have traditionally been transfused to achieve and maintain an Hb concentration of 100 g/l but, in the absence of significant heart disease, a target of 70–90 g/l may be preferable (Box 24.19, p. 1019).

Fluid challenges of 200–250 ml should be titrated against CVP measurements (Fig. 8.1, p. 180).

When the preload is high, due to excessive intravascular volume or impaired myocardial contractility, it is advisable to remove volume from the circulation (diuretics, vasoconstriction, haemofiltration) or increase the capacity of the vascular bed using venodilator therapy (glyceryl trinitrate, morphine).

8.14 INITIAL MANAGEMENT OF CIRCULATORY COLLAPSE

● Monitor MAP, CVP
● Correct hypovolaemia if CVP < 6 mmHg from mid-axillary line give volume challenge (250 ml normal saline or colloid)
● Correct hypotension if CVP < +6 mmHg or poor ventricular function is suspected, use only 100 ml of fluid and consider insertion of PA catheter to direct further treatment with fluids and vasoactive agents
● Achieve target MAP (using vasoactive agents only after hypovolaemia corrected)
● Monitor trend in arterial blood gases, pH, base deficit and lactate
● Consider intubation if Paco₂ > 6.5 kPa (> 50 mmHg) Respiratory rate > 25/min Impaired consciousness: GCS ≤ 7
● Correct acidemia with i.v. bicarbonate if H⁺ > 63 mmol/l (pH < 7.20) and Paco₂ < 6 kPa (< 45 mmHg) (i.e. base excess > –10 mmol/l)

8.15 FACTORS INFLUENCING CENTRAL VENOUS PRESSURE

● Intravascular volume
● Venous tone
● Right heart function and ‘afterload’, i.e. PAP
● Intrathoracic pressure
**AFTERLOAD**

The tension in the ventricular myocardium during systole, or ‘afterload’, is determined by the resistance to ventricular outflow, which is a function of the peripheral arteriolar resistance. If the considerable assumption is made that flow in the circulation is linear and non-pulsatile, the resistance against which each ventricle works may be calculated as the pressure drop across the resistance bed divided by the flow:

Systemic vascular resistance (SVR) = (MAP – RAP)/Q
Pulmonary vascular resistance (PVR) = (PAP – LAP)/Q

If the pressures are measured in mmHg and flow in litres/min, these calculations give the resistances in simple or ‘Wood’ units; multiplication by 80 converts to SI units. For a normal 70 kg adult:

SVR = (90 – 0)/5 × 80 = 1440 dyn.sec/cm^5
PVR = (10 – 5)/5 × 80 = 80 dyn.sec/cm^5

Understanding the reciprocal relationship between pressure, flow and resistance is crucial for appropriate circulatory management. High resistances produce lower flows at higher pressures for a given amount of ventricular work. Therefore, a systemic vasodilator such as sodium nitroprusside will allow the same cardiac output to be maintained for less ventricular work but with a reduced arterial blood pressure. In hyperdynamic sepsis, the SVR and blood pressure are low but the cardiac output is high; therefore a vasoconstrictor (noradrenaline (norepinephrine), vasopressin) is appropriate to restore BP, albeit with some reduction in cardiac output.

**MYOCARDIAL CONTRACTILITY**

This determines the work that the ventricle performs under given loading conditions or, put another way, the stroke volume that the ventricle will generate against a given afterload for a particular level of preload.

The relationship between stroke work and filling pressure is shown in Figure 18.21, page 543. The ventricular stroke work is the external work performed by the ventricle with each beat and is calculated from the stroke volume (SV) and the pre- and afterload pressures:

Ventricular stroke work (VSW) = SV × (afterload – preload)

e.g. LVSW = SV × (MAP – LAP) ml.mmHg

Using the data for a normal adult shown in Box 8.6 (p. 186) and multiplying by 0.0136 to convert to SI units of gram.metres, LVSW and RVSW are 80 and 10 g.m respectively.

Consideration of ventricular work is important because it is desirable to maintain satisfactory perfusion and oxygen delivery to all organs at maximum cardiac efficiency and therefore minimise myocardial ischaemia. Myocardial contractility is frequently reduced in critically ill patients due to either pre-existing cardiac disease (usually ischaemic heart disease) or the disease process itself (particularly sepsis).

**THERAPEUTIC OPTIONS IN THE MANAGEMENT OF CARDIAC FAILURE**

If the cardiac output is inadequate and myocardial contractility is poor, the available treatment options are to:

- **Reduce afterload.** This can be achieved by using an arteriolar dilator (e.g. nitrates, ACE inhibitor), which may be limited by the consequent fall in systemic pressure. A counterpulsation balloon pump offers the ideal physiological treatment because it reduces LV afterload while increasing cardiac output, diastolic pressure and coronary perfusion; it is particularly valuable in treating myocardial ischaemia.

---

**8.16 CIRCULATORY EFFECTS OF COMMONLY USED VASODILATING DRUG INFUSIONS**

<table>
<thead>
<tr>
<th>Drug (receptors)</th>
<th>Cardiac contractility</th>
<th>Heart rate</th>
<th>Blood pressure</th>
<th>Cardiac output</th>
<th>Splanchnic blood flow</th>
<th>SVR</th>
<th>PVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine (&lt; 5 μg/kg/min (DA1, β1, α) ➞ 5 μg/kg/min (β2, DA1, DA2))</td>
<td>↑↑</td>
<td>−/↑</td>
<td>−/↑</td>
<td>↑↑</td>
<td>−/↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Adrenaline (epinephrine) (β1, β2)</td>
<td>↑↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Noradrenaline (norepinephrine) (α1, β2)</td>
<td>−/↑</td>
<td>−/↓</td>
<td>↑</td>
<td>−/↓</td>
<td>−/↓</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Isoprenaline (β1, β2)</td>
<td>↑</td>
<td>↑</td>
<td>−/↓</td>
<td>↑</td>
<td>−/↑</td>
<td>−/↓</td>
<td>↓</td>
</tr>
<tr>
<td>Dobutamine (β1, β2, α)</td>
<td>↑</td>
<td>↑</td>
<td>−/↓</td>
<td>↑</td>
<td>−/↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Dopexamine (β2, DA1, DA2)</td>
<td>↑</td>
<td>↑</td>
<td>−/↓</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Glyceryl trinitrate (NO)</td>
<td>➞</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Nitroprusside (NO)</td>
<td>➞</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Epoprostenol (prostacyclin)</td>
<td>➞</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Milrinone (PDEI)</td>
<td>➞</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
</tr>
</tbody>
</table>

Receptors through which these vasodilating drugs work are given in parentheses and listed in order of the extent of receptor stimulation produced. Note that dopamine acts more like adrenaline at high doses. (α = α-adrenoceptor; β1, β2 = β-adrenoceptors 1 and 2; DA1, DA2 = dopaminergic receptors 1 and 2; NO = NO acts via local nitric oxide release; PDEI = phosphodiesterase inhibitor.)

The global circulatory effects listed are guidelines only. The magnitude of the response will depend on the circulatory state of the patient when the drug is started, the dose of the drug administered and the receptor distribution and density in specific vascular beds.
● Increase preload. However, if there is significant impairment of myocardial contractility, giving intravascular volume to increase filling pressures will only produce a small increase in stroke volume and cardiac output and risks precipitating pulmonary oedema.
● Improve myocardial contractility. Box 8.16. lists some characteristics of the commonly used inotropic agents.
● Control heart rate and rhythm (pp. 356–75). The optimum heart rate is usually between 90 and 110 per minute. Correction of low serum potassium and magnesium concentrations should be the first stage in treating tachyarrhythmias in the critically ill. Atrial fibrillation is particularly common and troublesome in septic and critically ill patients; amiodarone 300 mg over 30–60 minutes, followed by 900 mg over 24 hours, can be successful in controlling ventricular rate and in restoring and maintaining sinus rhythm.

The management of tamponade and pulmonary embolism is described on pages 645 and 724 respectively and specific aspects of management in sepsis are described later (p. 199).

RESPIRATORY SUPPORT

Respiratory support is indicated to maintain the patency of the airway, correct hypoxaemia and hypercapnia, and reduce the work of breathing. It ranges from oxygen therapy by facemask, through non-invasive techniques such as CPAP (Box 8.17) and non-invasive positive pressure ventilation (NIPPV), to full ventilation via an endotracheal tube or tracheostomy.

OXYGEN THERAPY

Oxygen is given to treat hypoxaemia and ensure adequate arterial oxygenation ($SpO_2 > 90\%$). It should initially be given by facemask or nasal cannulae and the inspired oxygen concentration ($FIO_2$) can then be adjusted according to the results of pulse oximetry and arterial blood gas analysis. The risk of progressive hypercapnia in certain patients with COPD who are dependent on hypoxic drive has been overstated. If administration of oxygen to ensure $SpO_2 > 90\%$ results in unacceptable hypercapnia, the patient almost certainly requires some form of mechanical respiratory support. The theoretical risks of oxygen toxicity are not relevant if the patient is acutely hypoxaemic. It is vital to maintain cerebral oxygenation even at the risk of pulmonary toxicity because hypoxic cerebral damage is irreversible. More detail on oxygen therapy is given on page 668.

NON-INVASIVE RESPIRATORY SUPPORT

If a patient remains hypoxaemic on high-flow oxygen, other measures are required to improve oxygenation and to reduce the work of breathing. If the patient has respiratory failure associated with decreased lung volume, application of continuous positive airways pressure (CPAP, Box 8.17) will both improve oxygenation by recruitment of under-ventilated alveoli, and reduce the work of breathing by

<table>
<thead>
<tr>
<th>8.17 MODES AND TERMS USED IN MECHANICAL VENTILATORY SUPPORT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intermittent positive pressure ventilation (IPPV)</strong></td>
</tr>
<tr>
<td>● Generic term for all types of positive pressure ventilation</td>
</tr>
<tr>
<td><strong>Controlled mandatory ventilation (CMV)</strong></td>
</tr>
<tr>
<td>● Most basic classic form of ventilation</td>
</tr>
<tr>
<td>● Pre-set rate and tidal volume</td>
</tr>
<tr>
<td>● Does not allow spontaneous breaths</td>
</tr>
<tr>
<td>● Appropriate for initial control of patients with little respiratory drive, severe lung injury or circulatory instability</td>
</tr>
<tr>
<td><strong>Synchronous intermittent mandatory ventilation (SIMV)</strong></td>
</tr>
<tr>
<td>● Pre-set rate of mandatory breaths with pre-set tidal volume</td>
</tr>
<tr>
<td>● Allows spontaneous breaths between mandatory breaths</td>
</tr>
<tr>
<td>● Allows patient to settle on ventilator with less sedation</td>
</tr>
<tr>
<td><strong>Pressure controlled ventilation (PCV)</strong></td>
</tr>
<tr>
<td>● Pre-set rate; pre-set inspiratory pressure</td>
</tr>
<tr>
<td>● Tidal volume depends on pre-set pressure, lung compliance and airways resistance</td>
</tr>
<tr>
<td>● Used in management of severe acute respiratory failure to avoid high airway pressure, often with prolonged inspiratory to expiratory ratio (pressure controlled inverse ratio ventilation, PCIRV)</td>
</tr>
<tr>
<td><strong>Pressure support ventilation (PSV)</strong></td>
</tr>
<tr>
<td>● Breaths are triggered by patient</td>
</tr>
<tr>
<td>● Provides positive pressure to augment patient’s breaths</td>
</tr>
<tr>
<td>● Useful for weaning</td>
</tr>
<tr>
<td>● Usually combined with CPAP: may be combined with SIMV</td>
</tr>
<tr>
<td>● Pressure support is titrated against tidal volume and respiratory rate</td>
</tr>
<tr>
<td><strong>Positive end-expiratory pressure (PEEP)</strong></td>
</tr>
<tr>
<td>● Positive airway pressure applied during expiratory phase in patients receiving mechanical ventilation</td>
</tr>
<tr>
<td>● Improves oxygenation by recruiting atelectatic or oedematous lung</td>
</tr>
<tr>
<td>● May impair venous return and reduce cardiac output</td>
</tr>
<tr>
<td><strong>Continuous positive airways pressure (CPAP)</strong></td>
</tr>
<tr>
<td>● Positive airway pressure applied throughout the respiratory cycle, via either an endotracheal tube or a tight-fitting facemask</td>
</tr>
<tr>
<td>● Fresh gas flow must exceed patient’s peak inspiratory flow</td>
</tr>
<tr>
<td>● Improves oxygenation by recruitment of atelectatic or oedematous lung</td>
</tr>
<tr>
<td>● Mask CPAP discourages coughing and clearance of lung secretions; may increase the risk of aspiration</td>
</tr>
<tr>
<td><strong>Bi-level positive airway pressure (BiPAP/BIPAP)</strong></td>
</tr>
<tr>
<td>● Describes situation of two levels of positive airway pressure (higher level in inspiration)</td>
</tr>
<tr>
<td>● In fully ventilated patients, BiPAP is essentially the same as PCV with PEEP</td>
</tr>
<tr>
<td>● In partially ventilated patients, and especially if used non-invasively, BiPAP is essentially PSV with CPAP</td>
</tr>
<tr>
<td><strong>Non-invasive intermittent positive pressure ventilation (NIPPV)</strong></td>
</tr>
<tr>
<td>● Most modes of ventilation may be applied via a facemask or nasal mask</td>
</tr>
<tr>
<td>● Usually PSV/BiPAP (typically 15–20 cmH2O) often with back-up mandatory rate</td>
</tr>
<tr>
<td>● Indications include acute exacerbations of COPD</td>
</tr>
</tbody>
</table>
improving lung compliance. CPAP is most successful in clinical situations where alveoli are readily recruited, such as in pulmonary oedema and post-operative collapse/atelectasis. It is also helpful in treating pneumonia, especially in immunocompromised patients. The risk of nosocomial infection is reduced by avoiding endotracheal intubation. A CPAP mask often becomes uncomfortable and gastric distension may occur. Patients must therefore be cooperative, be able to protect their airway and have the strength to breathe spontaneously and cough effectively.

NIPPV refers to ventilatory support by nasal or full facemask. It may avoid the need for endotracheal intubation in patients with type 2 respiratory failure, typically those with exacerbations of COPD, and it may be used during weaning from conventional ventilation. As with mask CPAP, NIPPV requires the patient to be conscious and cooperative.

**ENDOTRACHEAL INTUBATION AND MECHANICAL VENTILATION**

Over 60% of patients appropriately admitted to ICU require endotracheal intubation and mechanical ventilation, mostly for respiratory failure but also for other reasons (Boxes 8.18 and 8.19).

The final decision to perform tracheal intubation and ventilate a patient should be taken on clinical grounds rather than as a response to the results of particular investigations.

In the conscious patient, intubation requires induction of anaesthesia and muscle relaxation, while in more obtunded patients sedation alone may be adequate. This can be hazardous in the critically ill patient with respiratory and often cardiovascular failure. Continuous monitoring, particularly of heart rate and BP (preferably invasively), is essential, and resuscitation drugs must be immediately available. Hypotension commonly follows sedation or anaesthesia because of direct cardiovascular effects of the drugs and loss of sympathetic drive; positive pressure ventilation may compound this problem by increasing intrathoracic pressure, thereby reducing venous return and hence cardiac output.

The different types of ventilatory support are illustrated in Figure 8.9. Modern ventilators allow considerable flexibility in the level of support from controlled mandatory ventilation to partial ventilatory support modes, and assisted spontaneous breathing which allows the ventilator to respond to patients’ demands. Use of partial ventilatory support avoids the requirement for and hazards of paralysis and deep sedation, and allows the patient to be conscious and yet comfortable.
General considerations in the management of the ventilated/intubated patient

- Beware of the restless patient. Try to establish the cause of the problem before simply administering sedation. Possibilities include pneumothorax, hypoxaemia, hypercapnia due to inadequate ventilation, pain, onset of sepsis, cardiac decompensation (pulmonary oedema, dysrhythmia, infarction) and proximal airway obstruction, e.g. secretions.

- Patients who are breathing spontaneously adjust their ventilation to compensate for metabolic derangements; this cannot occur in patients who are ventilated using mandatory modes so the clinician must either correct the underlying metabolic abnormality or make appropriate changes to the ventilator settings. For example, a patient with severe diabetic ketoacidosis will hyperventilate to compensate for the metabolic acidosis; if mechanical ventilation is instituted, there will be a potentially catastrophic fall in pH unless the acidosis is corrected by administering sodium bicarbonate or a high minute volume (artificial hyperventilation) is delivered.

- Ventilator should be set to detect:
  - minimum acceptable minute volume to identify inadvertent disconnection
  - maximum acceptable airway pressure to prevent barotrauma.

- Humidify and warm inspired gas to prevent inspissation of secretions.

- Arrange regular positioning, physiotherapy and suctioning to clear secretions and prevent proximal airway obstruction and distal alveolar collapse. The patient should be in a 30° head-up position to avoid aspiration.

- Obtain a chest X-ray to check the position of the endotracheal tube following intubation (the appropriate position is 4 cm above the carina).

- Bronchoscopy should be readily available to:
  - investigate upper airways obstruction (plugging of the proximal bronchial tree by inspissated mucus is the most common cause)
  - investigate lobar/segmental collapse, and aspirate mucus plug obstructing proximal bronchial tree
  - assist in cases of difficult intubation or tracheostomy tube change
  - obtain bronchoalveolar lavage specimens for microbiology
  - identify the cause of haemoptysis (not always easy)
  - exclude tracheobronchial disruption after thoracic trauma.

Ventilation strategy

The selection of ventilator mode and settings for tidal volume, respiratory rate, positive end-expiratory pressure (PEEP) and inspiratory to expiratory ratio is dependent on the cause of the respiratory failure. The objectives are to:

- improve gas exchange
- minimise damage to the lung by avoiding high lung volumes and $\text{FiO}_2$
- avoid adverse circulatory effects
- make the patient comfortable without heavy sedation or muscle paralysis by reducing the work of breathing and harmonising interaction between patient and ventilator.

In asthma and conditions with increased lung volumes (high FRC) a prolonged expiratory phase is necessary to prevent progressive lung over-inflation; PEEP and large tidal volumes exacerbate over-distension, produce high alveolar pressures and increase the risk of pneumothorax. High intrathoracic pressures compromise circulatory function, particularly if there is intravascular volume depletion, so that oxygen delivery may actually fall in spite of improved arterial oxygenation.

In patients with alveolar collapse (low FRC), such as those with ARDS, it is appropriate to use a prolonged inspiratory to expiratory ratio and high levels of PEEP (+10 to +15 cm$\text{H}_2\text{O}$) to recruit alveoli and improve compliance and gas exchange (Boxes 8.20 and 8.21). Recent studies have shown that in ARDS, damage to the lungs can be exacerbated by mechanical ventilation, possibly by over-distension of alveoli and repeated opening and closure of distal airways.

Other management strategies which may be of benefit in severe ARDS include prone ventilation, nitric oxide inhalation and corticosteroids.

Prone ventilation

Prone positioning improves oxygenation significantly in two-thirds of patients with ARDS by reducing thoraco-abdominal compliance and the vertical pleural pressure gradient so that ventilation is more evenly distributed and better matched to perfusion. Multicentre trials using manual pronation have failed to show a survival benefit and trials using an automatic rotating bed are underway.

8.20 PRINCIPLES OF MECHANICAL VENTILATION IN ARDS

- Optimum ventilator settings are:
  - Pressure-controlled
  - Long inspiratory to expiratory time
  - Positive end-expiratory pressure (PEEP)
  - Allow $\text{PaCO}_2$ to rise (permissive hypercapnia) and tolerate lower oxygen saturations than normal (e.g. 88–90%)
  - Avoid:
    - Large tidal volumes (ideally 6 ml/kg)
    - Airway pressures of more than 35 cm$\text{H}_2\text{O}$
    - $\text{FiO}_2$ of more than 0.8 if possible
  - Remember that high intrathoracic pressures compromise circulatory function so oxygen delivery may actually fall in spite of improved oxygenation
  - Management must be a balance between improving gas exchange, minimising the risk of subsequent pulmonary fibrosis due to lung injury, and avoiding adverse circulatory effects

8.21 OPTIMAL VENTILATION IN ARDS

"Ventilation using positive end-expiratory pressure but limiting tidal volumes to 5–7 ml/kg and accepting high $\text{PaCO}_2$ levels improves outcome in ARDS."

Inhaled nitric oxide

Nitric oxide is a very short-acting pulmonary vasodilator. Delivered to the airway in concentrations of between 1 and 20 parts per million, it improves blood flow to ventilated alveoli, thus improving ventilation–perfusion matching. Oxygenation can be improved markedly in some patients but the evidence indicates that the benefit only lasts for 48 hours and outcome is not improved.

Pharmacological therapy

There is now considerable evidence that corticosteroids improve outcome if given in the fibroproliferative stage of ARDS. A trial of corticosteroids is therefore indicated if a patient with ARDS has consistent gas exchange impairment and ventilator dependence at 7–10 days after diagnosis. The recommended dose of methylprednisolone is 2–3 mg/kg/day, decreasing after 7 days and as gas exchange improves. Bronchoscopy and bronchoalveolar lavage should be performed to identify or exclude pulmonary infection before commencing corticosteroid therapy.

Weaning from respiratory support

This is the process of progressively reducing and eventually removing all external ventilatory support and associated apparatus. The majority of patients require mechanical ventilatory support for only a few days and do not need weaning. In these patients simple trials of spontaneous breathing via the endotracheal tube will usually indicate whether the patient can be successfully extubated or not.

In contrast, patients who have required long-term ventilatory support for severe lung disease, e.g. ARDS, may initially be unable to sustain even a modest degree of respiratory work because of residual decreased lung compliance and hence increased work of breathing, compounded by respiratory muscle weakness. These patients therefore require weaning until respiratory muscle strength improves to the point that all support can be discontinued.

Weaning techniques involve the patient breathing spontaneously for increasing periods of the day and a gradual reduction in the level of ventilatory support. This often involves graduation to partial support modes and then non-invasive modes of ventilatory support.

Increasingly, the process of identifying patients able to progress to spontaneous breathing and extubation is done according to a ‘weaning protocol’. This entails deciding whether a patient can be safely subjected to a spontaneous breathing trial (Box 8.22). If the patient meets the criteria listed, he or she undergoes the breathing trial for 2–5 minutes. The respiratory rate and tidal volume are noted, and the ratio calculated. If it is less than 105 breaths/min/litre, the patient continues the trial for a further 30 minutes to 2 hours period before extubation.

In the event of failure (increased respiratory rate; decreased tidal volume) gradual weaning of ventilation continues using synchronised intermittent mandatory ventilation (SIMV), pressure support ventilation (PSV) or intermittent periods of spontaneous breathing. Non-invasive ventilation via a facemask can allow earlier extubation in certain groups of patients, e.g. chronic obstructive pulmonary disease, with weaning continuing after removal of the endotracheal tube.

Despite the development of a number of objective tests and indices of the patient’s ability to sustain spontaneous ventilation, the decision to extubate and the speed of weaning from mechanical ventilation still rely largely on clinical judgement.

Tracheostomy

Tracheostomy is usually performed electively when endotracheal intubation is likely to be prolonged (over 14 days). Tracheostomies have benefits in terms of patient comfort, aid weaning from ventilation (since sedation can be reduced or stopped), and allow access for tracheal toilet and intermittent respiratory support (Box 8.23).

Tracheostomy is now usually carried out using a percutaneous technique in the ICU, which avoids the need for transfer to the operating theatre. This has led to earlier and more frequent use of tracheostomy. Preliminary evidence indicates that early tracheostomy (at < 3 days) in patients predicted to require prolonged ventilation leads to a reduced length of ICU stay, and decreased morbidity and mortality.

Mini-tracheostomy

The passage of a smaller (4.5 mm internal diameter) tube through the cricothyroid membrane is a useful technique to clear airway secretions in spontaneously breathing patients with a poor cough effort. It can be particularly useful in the HDU and in post-operative patients.

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**8.22 FACTORS IN DECIDING WHETHER A VENTILATED PATIENT CAN BE WEANED AND SAFELY EXTUBATED**

- Has the original indication for mechanical ventilation resolved?
- Is the patient conscious and able to cough and protect his/her airway?
- Is the circulation stable, with a normal or reasonably low left atrial pressure?
- Is gas exchange satisfactory (PaO₂ > 8 kPa (> 60 mmHg) on FiO₂ < 0.5; PaCO₂ < 6 kPa (< 45 mmHg))?
- Is analgesia adequate?
- Are any metabolic problems well controlled?

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**8.23 ADVANTAGES AND DISADVANTAGES OF TRACHEOSTOMY**

**Advantages**

- Patient comfort
- Improved oral hygiene
- Reduced sedation requirement
- Enables speech with cuff deflated and a speaking valve attached
- Earlier weaning and ICU discharge
- Access for tracheal toilet
- Reduces vocal cord damage

**Disadvantages**

- Immediate complications: hypoxia, haemorrhage
- Tracheal damage; late stenosis
- Tracheostomy site infection
RENAL SUPPORT

Oliguria (<0.5 ml/kg/hr for 2–3 hours) requires explanation and early intervention to correct hypoxaemia, hypovolaemia, hypotension and renal hyperperfusion. There is little evidence that specific treatments aimed at inducing a diuresis, such as low-dose dopamine, furosemide or mannitol, have remprotective action or additional beneficial value in restoring renal function beyond aggressive haemodynamic resuscitation to achieve normovolaemia, normotension and an appropriate cardiac output. Sepsis is frequently implicated in the development of acute renal failure and the focus must be promptly and adequately treated by surgical drainage and antibiotics if renal function is to be restored. Obstruction of the renal tract should always be excluded by abdominal ultrasound and, if present, should be relieved.

If renal function cannot be restored following resuscitation, renal replacement therapy (p. 491) is indicated (Box 8.24).

8.24 INDICATIONS FOR RENAL REPLACEMENT THERAPY

- Fluid overload: pulmonary oedema
- Hyperkalaemia: potassium > 6 mmol/l despite medical management
- Metabolic acidosis: H+ > 56 nmol/l (pH < 7.25)
- Uraemia:
  - Urea > 30–35 mmol/l (180–210 mg/dl)
  - Creatinine > 600 μmol/l (> 6.78 mg/dl)
- Drug removal, in overdose situations
- Sepsis: tentative evidence for mediator removal

The preferred renal replacement therapy in ICU patients is pumped venovenous haemofiltration. This is associated with fewer osmotic fluid shifts and hence greater haemodynamic stability than haemodialysis. It is carried out using a double-lumen central venous catheter placed percutaneously. Haemofiltration should be continuous; higher rates of filtration (preferably > 35 ml/kg/hr) are associated with improved outcome. Intermittent treatment should only be used when the patient is recovering from the primary insult and return of normal renal function is expected. Provided the precipitating cause can be successfully treated, renal failure due to ATN usually recovers between 5 days and several weeks later.

Survival rates from multiple organ failure including acute renal failure have been around 50% for many years but recent evidence suggests that modern haemofiltration techniques are producing better outcomes.

GASTROINTESTINAL AND HEPATIC SUPPORT

The gastrointestinal tract and liver play an important role in the evolution of multiple organ failure, even when the primary diagnosis is not related to the abdomen. Gastrointestinal symptoms such as nausea, vomiting and large nasogastric aspirates may be the earliest signs of regional circulatory failure and, when associated with a tender, distended, silent abdomen, indicate the probable site of the primary pathology. Ischaemic bowel is difficult to diagnose in the critically ill patient but, in the context of an otherwise unexplained lactic acidosis, hyperkalaemia and coagulopathy, urgent laparotomy must be considered (p. 922).

The gut has a very rapid cell turnover rate and fasting alone can produce marked changes in mucosal structure and function. In hypovolaemic and frank shock states, splanchnic vasoconstriction produces gut mucosal ischaemia, damaging the mucosal barrier and allowing toxins to enter the portal circulation and lymphatics. Although equipped to cope with moderate portal toxaemia, the liver may be overwhelmed and then augment the inflammatory response itself by releasing cytokines into the systemic circulation. For this reason the gut has been described as the ‘undrained abscess’ or ‘motor of multiple organ failure.’

Manifestations of MOF within the gastrointestinal tract include erosive gastritis, stress ulceration, bleeding, ischaemia, pancreatitis and acalculous cholecystitis. Adequacy of gastric mucosal perfusion can be assessed by gastric tonometry, a technique that uses a modified nasogastric tube with a balloon containing either saline or air to measure intramucosal pH (pHi) or PCO2i. An increased difference between gastric PCO2 and arterial PCO2 or an intramucosal acidosis (pHi < 7.32) implies mucosal ischaemia.

Early institution of enteral nutrition is the most effective strategy for protecting the gut mucosa and providing nutritional support. There is evidence suggesting that nasogastric feeds supplemented with arginine, omega 3 fatty acids and nucleotides (‘immunonutrition’) may improve outcome in critical illness. Glutamine supplementation is logical, although not of proven benefit, since it is a ‘conditionally essential’ amino acid and the principal energy substrate used by the gut mucosa in critical illness. Total parenteral nutrition (TPN) should only be started if all attempts at implementing enteral feeding, including nasojejunal delivery, have failed; it should be necessary in fewer than 10% of general ICU patients.

Recent evidence from a randomised controlled trial (RCT) demonstrates improved outcomes in the critically ill resulting from tight glycaemic control (Box 8.25). Many patients in ICU will require insulin to maintain a blood sugar between 4.5 and 6.5 mmol/l (~ 80–120 mg/dl), when on either enteral or parenteral feeding.

Ranitidine and sucralfate are both used to reduce the risk of gastrointestinal haemorrhage, although ranitidine is the more effective. Both agents are associated with an increased
incidence of nosocomial pneumonia. Treatment should be stopped when full enteral nutrition has been established and is probably only necessary in patients with a history of peptic ulcer and those who have evidence of MOF, and particularly severe coagulopathy.

The hepatic circulation, 80% of which is derived from the portal venous system, is compromised by the same factors which lead to splanchnic vasoconstriction. Hepatic ischaemia leads to impaired filtering of endotoxin from the portal circulation and, as SIRS develops, inflammatory mediators (e.g. cytokines IL-1, IL-6 and TNF) are released from activated Kupffer cells (hepatic macrophages) into the systemic circulation, increasing the risk of acute renal failure and the other manifestations of MOF developing. Increased metabolic activity in the liver as a result of sepsis and the need for vasoconstricting agents to maintain blood pressure increase hepatic ischaemia. The synthetic inodilator doxapamine with dopaminergic 1 and 2 and β-adrenergic effects may enhance splanchnic blood flow but has not been shown to improve outcome.

Two distinctive hepatic dysfunction syndromes occur in the critically ill:

- **Shock liver or ischaemic hepatitis** results from extreme hepatic tissue hypoxia and is characterised by centrilobular hepatocellular necrosis. Transaminase levels are often massively raised (> 1000–5000 U/l) at an early stage, followed by moderate hyperbilirubinaemia (< 100 μmol/l, < 5.8 mg/dl). There is often associated hypoglycaemia, coagulopathy and lactic acidosis. Following successful resuscitation, hepatic function generally returns to normal.

- **Hyperbilirubinaemia (‘ICU jaundice’)** frequently develops following trauma or sepsis, particularly if there is inadequate control of the inflammatory process. There is a marked rise in bilirubin levels (predominantly conjugated) but only mild elevation of transaminase and alkaline phosphatase levels. This results from failure of bilirubin transport within the liver and produces the histological appearance of intrahepatic cholestasis. Extrahepatic cholestasis must be excluded by abdominal ultrasound and potentially hepatotoxic drugs should be stopped. Treatment is non-specific and should include early institution of enteral feeding. Therapy that compromises splanchnic blood flow, particularly high doses of vasoconstrictor agents, should be avoided.

### NEUROLOGICAL SUPPORT

A diverse range of primary neurological and metabolic conditions require management in the ICU. These include the various causes of coma, spinal cord injury, peripheral neuromuscular disease and prolonged seizures. Intensive care is required to:

- manage acute brain injury with control of raised intracranial pressure
- protect the airway, if necessary by endotracheal intubation
- provide respiratory support to correct hypoxaemia and hypercapnia
- treat circulatory problems, e.g. neurogenic pulmonary oedema in subarachnoid haemorrhage, autonomic disturbances in Guillain–Barré syndrome, spinal shock following high spinal cord injuries
- manage status epilepticus using anaesthetic agents such as thiopental or propofol.

The aim of management in acute brain injury is to optimise cerebral oxygen delivery by maintaining a normal arterial oxygen content and a cerebral perfusion pressure above 70 mmHg. Avoiding secondary insults to the brain such as hypoxaemia and hypotension improves outcome in head injury. Intracranial pressure (ICP) rises in acute brain injury as a result of haematoma, contusions or ischaemic swelling. Raised ICP is damaging both directly to the cerebral cortex and by producing downward pressure on the brain stem, and indirectly by reducing cerebral perfusion pressure, thereby threatening cerebral blood flow and oxygen delivery:

Cerebral perfusion pressure (CPP) = mean BP – ICP

ICP may be measured via pressure transducers inserted directly into the brain tissue or held in place on the dura. The normal upper limit for ICP is 15 mmHg and management should be directed at keeping ICP below 20 mmHg (Box 8.26). Sustained pressures above 30 mmHg are associated with a poor prognosis.

Cerebral perfusion pressure should be maintained above 70 mmHg by ensuring adequate fluid replacement and if necessary by treating hypotension with a vasopressor such as noradrenaline (norepinephrine).

Complex neurological monitoring must be combined with frequent clinical assessment, i.e. GCS, pupil response to light and focal neurological signs. The motor response to pain is a particularly important prognostic sign. No response or extension of the upper limbs is associated with severe injury, and unless there is improvement within a few days prognosis is very poor. A flexor response is encouraging and indicates that a good outcome is still possible.

### 8.26 STRATEGIES TO CONTROL INTRACRANIAL PRESSURE

- Sedation, analgesia and occasionally paralysis to prevent coughing
- Nurse with 30° head-up tilt and avoid excessive flexion of the head or pressure around the neck that may impair cerebral venous drainage
- Control epileptiform activity with appropriate anticonvulsant therapy; an electroencephalogram (EEG) may be necessary to ensure this is achieved
- Maintain strict glycaemic control with blood glucose between 4 and 8 mmol/l (~ 70–140 mg/dl)
- Aim for a core body temperature of between 36 and 37°C
- Maintain sodium > 140 mmol/l using i.v. normal saline
- Avoid dehydration or fluid overload
- Hyperventilation to reduce the Pco2, to 4–4.5 kPa (~ 30–34 mmHg) for the first 24 hours
- Osmotic diuretic, mannitol 20% 100–200 ml (0.25–0.5 g/kg), coupled with volume replacement
- Hypnotic infusion, thiopental, titrated to ‘burst suppression’ on EEG
- Surgery: drainage of haematoma or ventricles; lobectomy, decompressive craniectomy
NEUROLOGICAL COMPLICATIONS IN INTENSIVE CARE

Neurological complications also occur as a result of systemic critical illness. Sepsis may be associated with an encephalopathy characterised by confusion/delirium and associated with cerebral oedema and loss of vasoregulation. Hypotension and coagulopathy may provoke cerebral infarction or haemorrhage. Neurological examination is very difficult if the patient is sedated or paralysed and it is important to stop sedation regularly to reassess the patient’s underlying level of consciousness. If there is evidence of a focal neurological deficit or a markedly declining level of consciousness, a CT of the brain should be performed.

Critical illness polyneuropathy is another potential complication in patients with sepsis and MOF. It is due to peripheral nerve axonal loss rather than demyelination and can result in areflexia, gross muscle-wasting and failure to wean from the ventilator, thus prolonging the duration of intensive care. Recovery can take many weeks.

MANAGEMENT OF SEPSIS

Prompt administration of appropriate antibiotics with a spectrum wide enough to cover probable causative organisms, based on an analysis of the likely site of infection, previous antibiotic therapy and the known resistance patterns on the unit, is essential. The haemodynamic changes in septic shock are very variable and are not specific for the Gram status of the infecting organism. The early stages of septic shock are often dominated by hypotension with relative volume depletion due to marked arteriolar and particularly venular dilatation. Sufficient intravenous fluid should be given to ensure that the intravascular volume is not the limiting factor in determining global oxygen delivery. The type of fluid that should be administered and what constitutes ‘adequate’ volume resuscitation remain controversial. The response to therapy is crucial and frequently unpredictable so it is not appropriate to use rigid protocols. While the patient remains clinically volume-depleted, a continuous crystalloid infusion of at least 1–2 ml/kg/hr should be given, together with full enteral nutrition if tolerated to achieve the planned 24-hour crystalloid balance. Depending on haemoglobin concentration, blood or synthetic colloid should be given as 100–200 ml boluses to assess BP response to volume and to achieve CVP or PAWP targets. A recent meta-analysis has confirmed that albumin should not routinely be used in the resuscitation of critically ill patients (p. 425).

Excessive fluid replacement in pursuit of ‘supranormal’ goals is not beneficial in patients with established organ failure (p. 184) and may be harmful, producing excessive tissue oedema.

Although ventricular function is frequently impaired, the characteristically low SVR ensures a high cardiac output (once the patient is adequately volume-resuscitated) albeit with low blood pressure.

The choice of the most appropriate vasoactive drug to use should be based on a full analysis of the circulation and knowledge of the different inotropic, dilating or constricting properties of these drugs (Box 8.16, p. 192). In most cases a vasoconstrictor such as noradrenaline (norepinephrine) is necessary to increase SVR and blood pressure, while an inotrope may be necessary to maintain cardiac output and prevent regional ischaemia. In the later stages of severe sepsis the essential problem is at the level of the microcirculation. Oxygen uptake and utilisation are impaired due to failure of the regional distribution of flow and direct cellular toxicity despite adequate global oxygen delivery. Tissue oxygenation may be improved and aerobic metabolism sustained by reducing demand, i.e. metabolic rate (Box 8.27).

SPECIFIC THERAPIES

Corticosteroids

Assessment of the pituitary–adrenal axis is difficult in the critically ill but in some series up to 30% of patients have adrenal insufficiency as assessed by baseline cortisol levels and the response to adrenocorticotropic hormone (ACTH). Corticosteroid replacement therapy is controversial; early studies using short-term, high-dose methylprednisolone showed no benefit but recent studies using lower-dose infusions of hydrocortisone (8 mg/hr) for longer periods (5 days) demonstrated reduced vasoconstrictor requirements in hyperdynamic sepsis and one study has shown an outcome benefit.

Activated protein C

Until recently, numerous large multicentre trials using anti-cytokine and other novel drug therapies to interrupt the inflammatory cascade had all produced disappointing results. However, administration of activated protein C (levels of which frequently fall in critical illness) has recently been shown to produce a substantial reduction in mortality in patients with SIRS (Box 8.28).
SURVIVING SEPSIS CAMPAIGN

The Surviving Sepsis Campaign was launched in 2004 by an international group of critical care and infectious diseases ‘experts’ representing 11 major organisations with the aim of reducing the worldwide mortality from sepsis by 25% within 5 years. After reviewing and grading the available evidence, the group produced guidelines in the form of packages of care or ‘sepsis bundles’, each covering an aspect of the care of patients with severe sepsis (Box 8.4, p. 185). The belief is that this approach will eliminate the variable and piecemeal application of new evidence. The guidelines will be updated regularly as new evidence emerges and both the implementation of the guidelines and the outcome from sepsis will be audited to assess the success of the initiative.

DISCHARGE FROM INTENSIVE CARE

Discharge is appropriate when the original indication for admission has resolved and the patient has sufficient physiological reserve to remain safe and continue his or her recovery without the facilities available in intensive care. For long-stay ICU patients who have been ventilator-dependent, ‘step-down’ to the HDU is appropriate. Discharges from ICU/HDU should preferably take place within normal working hours as there is frequently a lack of skills on the general wards and of suitable junior medical and nursing support out of hours and at weekends.

The shortage of ICU and HDU beds in most hospitals in the UK creates pressure for early discharge but it has been shown that readmission rates and hospital mortality increase if discharge occurs prematurely or out of normal working hours.

The critical care team should give the receiving team a detailed handover, provide a written summary with relevant recent investigations, remain available for advice, and ideally should visit the patient on the ward within the 24 hours after discharge.

WITHDRAWAL OF CARE

Withdrawal of support is appropriate when it is clear that the patient has no realistic prospect of recovery or of surviving with a quality of life that he or she would value. In these situations intensive care will only prolong the dying process and is therefore both futile and an inhumane waste of resources. Nevertheless, when active support is withdrawn, management should remain positive and be directed towards allowing the patient to die with dignity and as free from distress as possible. Patients’ wishes in this regard are paramount and increasing use is being made of advance directives or ‘living wills’. Communication with the patient, if possible, with the family, with the referring clinicians and between members of the critical care team is crucial (Ch. 1). Failure in this area damages working relations, causes stress and unrealistic expectations, and leads to subsequent unhappiness, anger and litigation.

BRAIN DEATH

The preconditions for considering brain-stem death and the criteria for establishing the diagnosis are listed on page 1187.

When formal criteria for brain-stem death are met it is clearly inappropriate to continue supporting life with mechanical ventilation and, at this stage, the possibility of organ donation should be considered. All intensive care clinicians have a responsibility to approach relatives to seek consent for organ donation, provided there is no contraindication to the use of the organs. This can be a very difficult task but is easier if the patient carried an organ donor card. In the UK each region has a team of transplant coordinators who can help with the process and will provide information and advice about the necessary tests.

SCORING SYSTEMS IN CRITICAL CARE

Admission and discharge criteria vary between units so it is important to define the characteristics of the patients admitted (case mix) in order to assess the effects of the care provided on the outcome achieved (Box 8.29).

Two systems are widely used to measure severity of illness:

- ‘APACHE’ II—Acute Physiology Assessment and Chronic Health Evaluation
- ‘SAPS’ 2—Simplified Acute Physiology Score.

These scores include assessment of certain admission characteristics (e.g. age and pre-existing organ dysfunction) and a variety of routine physiological measurements (e.g. temperature, blood pressure, GCS) that reflect the response of the patient to his or her illness. Predicted mortality figures by diagnosis have been calculated from large databases generated from a range of ICUs. These allow a particular unit to evaluate its performance compared to the reference ICUs by calculating standardised mortality ratios (SMRs) for each diagnostic group:

$$SMR = \frac{\text{observed mortality}}{\text{predicted mortality}}$$

A value of unity indicates the same performance as the reference ICUs while a value < 1 indicates a better than predicted outcome. A unit may have a high SMR in a certain diagnostic category and this would prompt investigation into how such patients were managed, with the intention of identifying aspects of care that could be improved.

When combined with the admission diagnosis, scoring systems have been shown to correlate well with the risk of

8.29 USES OF CRITICAL CARE SCORING SYSTEMS

- Comparison of the performance of different units
- Assessment of new therapies
- Assessment of changes in unit policies and management guidelines
- Measurement of the cost-effectiveness of care
hospital death. Such outcome predictions can never be 100% accurate and should be viewed as only one of many factors that the clinician considers when deciding whether or not further intervention is appropriate.

**COSTS OF INTENSIVE CARE**

Measuring the costs of intensive care is complex. The most widely used system is the Therapeutic Intervention Scoring System (TISS), which scores interventions and nursing activities for each day of admission and correlates reasonably well with detailed measurements of staff, equipment and drug costs incurred within the unit. Since it focuses on nurse-based interventions, TISS may also be used as an index of nurse dependency.

Current estimates of the daily cost of intensive care in the UK vary from £1000 to £2000, with high-dependency care accounting for approximately 50% and general ward care 20% of these costs. In the UK, less than 2% of total healthcare expenditure is spent on critical care.

**OUTCOME FROM CRITICAL CARE**

The most widely used measure to assess outcome from intensive care is mortality. This should be quoted at hospital discharge and at 28 days because mortality at the time of discharge from the unit will be influenced by the unit discharge policy. Mortality is also influenced by case mix, length of stay and organisational aspects of the unit.

The Kings Fund has emphasised the need to demonstrate long-term benefit to justify the increasing costs of critical care provision. Quality of life following discharge should be included in the evaluation of critical care but it is difficult to measure and interpret, not least because no objective pre-morbid assessment is possible with emergency admissions. However, several units in the UK now run follow-up clinics and have identified that there is a high incidence of physical and psychological problems affecting the patient and his or her family following ICU discharge.

**FURTHER INFORMATION**

**Books and journal articles**

**Websites**
- www.esicm.org Guidelines, recommendations, consensus conference reports.
- www.ics.ac.uk Clinical guidelines and standards for intensive care.
- www.survivingsepsis.org Surviving Sepsis website.