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THE INDISPENSABLE GUIDE TO
CRITICAL CARE MEDICINE

OXFORD HANDBOOK OF
CRITICAL CARE

SECOND EDITION

Covers the daily management
of problems in the ICU

Problem orientated

Detailed and authoritative

Mervyn Singer
Andrew R. Webb

Respiratory Therapy Techniques

Oxygen therapy

All critically ill patients should receive additional inspired oxygen on a 'more not less is best' philosophy.

Principles

High flow, high concentration oxygen should be given to any acutely dyspnoeic or hypoxaemic patient until accurate titration can be performed using arterial blood gas analysis.

In general, maintain SaO_2 >90%, though preferably >95%. Compromises may need to be made during acute on chronic hypoxaemic respiratory failure, or prolonged severe ARDS, when lower values may suffice provided tissue oxygen delivery is maintained.

All patients placed on mechanical ventilation should initially receive a high FIO_2 until accurate titration is performed using arterial blood gas analysis.

Apart from patients receiving hyperbaric O_2 therapy (e.g. for carbon monoxide poisoning, diving accidents), there is no need to maintain supranormal levels of PaO_2.

Cautions

A *small* proportion of patients in chronic Type II (hypoxaemic, hypercapnic) respiratory failure will develop apnoea if their central hypoxic drive is removed by supplemental oxygen. However, this is seldom (if ever) abrupt and a period of deterioration and increasing drowsiness will alert medical and nursing staff to consider either (i) FIO_2 reduction if overall condition allows, (ii) non-invasive or invasive mechanical ventilation if fatiguing or (iii) use of respiratory stimulants such as doxepram. The corollary is that close supervision and monitoring is necessary in all critically ill patients.

A normal pulse oximetry reading may obscure deteriorating gas exchange and progressive hypercapnia.

Oxygen toxicity is described in animal models. Normal volunteers will become symptomatic after several hours of breathing pure oxygen. Furthermore, washout of nitrogen may lead to microatelectasis. However, the relevance and relative importance of oxygen toxicity compared to other forms of ventilator trauma in critically ill patients is still far from clear. Efforts should nevertheless be made to minimise FIO_2 whenever possible. Debate continues as to whether FIO_2 or other ventilator settings (e.g. PEEP, V_T, inspiratory pressures) should be reduced first. The authors' present view is to minimise the risks of ventilator trauma.

Monitoring

An oxygen analyser in the inspiratory limb of the ventilator or CPAP/BiPAP circuit confirms the patient is receiving a known FIO_2. Most modern ventilators have a built-in calibration device.

Adequacy and changes in arterial oxygen saturation can be continuously monitored by pulse oximetry and intermittent or continuous invasive blood gas analysis.

Oxygen masks

- Hudson-type masks or nasal 'spectacles' give an imprecise FIO_2 and should only be used when hypoxaemia is not a major concern. Hudson-type masks do allow delivery of humidified gas (e.g. via an 'Aquapak'). Valves fitted to the Aquapak system do not deliver an accurate FIO_2 unless gas flow is at the recommended level.

- Masks fitted with a Venturi valve deliver a reasonably accurate FIO_2 (0.24, 0.28, 0.35, 0.40, 0.60) except in patients with very high inspiratory flow rates. These masks do not allow delivery of humidified gas but are preferable in the short term for dyspnoeic patients as they enable more precise monitoring of PaO_2/FIO_2 ratios.

- A tight-fitting anaesthetic mask and reservoir bag allows 100% oxygen to be delivered.

See also:

Ventilatory support—indications

Acute ventilatory insufficiency

Defined by an acute rise in $PaCO_2$ and a significant respiratory acidosis. $PaCO_2$ is directly proportional to the body's CO_2 production and inversely proportional to alveolar ventilation (minute ventilation minus dead space ventilation). Causes include:

- Respiratory centre depression, e.g. depressant drugs or intracranial pathology

- Peripheral neuromuscular disease, e.g. Guillain–Barré syndrome, myasthenia gravis or spinal cord pathology

- Therapeutic muscle paralysis, e.g. as part of balanced anaesthesia, for management of tetanus or status epilepticus

- Loss of chest wall integrity, e.g. chest trauma, diaphragm rupture

- High CO_2 production, e.g. burns, sepsis or severe agitation

- Reduced alveolar ventilation, e.g. airway obstruction (asthma, acute bronchitis, foreign body), atelectasis, pneumonia, pulmonary oedema (ARDS, cardiac failure), pleural pathology, fibrotic lung disease, obesity

- Pulmonary vascular disease (pulmonary embolus, cardiac failure, ARDS)

Oxygenation failure

Hypoxaemia is defined by PaO_2 <11kPa on $FIO_2 \geq 0.4$. May be due to:

- Ventilation–perfusion mismatching (reduced ventilation in, or preferential perfusion of, some lung areas), e.g. pneumonia, pulmonary oedema, pulmonary vascular disease, extremely high cardiac output

- Shunt (normal perfusion but absent ventilation in some lung zones), e.g. pneumonia, pulmonary oedema

- Diffusion limitation (reduced alveolar surface area with normal ventilation), e.g. emphysema; reduced inspired oxygen tension, e.g. altitude, suffocation

- Acute ventilatory insufficiency (as above)

To reduce intracranial pressure

Reduction of $PaCO_2$ to approximately 4kPa causes cerebral vasoconstriction and therefore reduces intracranial pressure after brain injury. Recent studies suggest this effect is transient and may impair an already critical cerebral blood flow.

To reduce work of breathing

Assisted ventilation ± sedation and muscle relaxation reduces respiratory muscle activity and thus the work of breathing. In cardiac failure or non-cardiogenic pulmonary oedema the resulting reduction in myocardial oxygen demand is more easily matched to the supply of oxygen.

Indications for ventilatory support

Ventilatory support (invasive or non-invasive) should be considered if:

Respiratory rate >30/min

Vital capacity <10–15ml/min

PaO_2 <11kPa on $FIO_2 \geq 0.4$

$PaCO_2$ high with significant respiratory acidosis (e.g. pH <7.2)

Vd/V_T >60%

Qs/Qt >15–20%

Exhaustion

Confusion

Severe shock

Severe LVF

Raised ICP

See also:

IPPV—description of ventilators

Classification of mechanical ventilators

These may be classified by the method of cycling from inspiration to expiration. This may be when a preset time has elapsed (time-cycled), a preset pressure reached (pressure-cycled) or a preset volume delivered (volume-cycled). Though the method of cycling is classified according to a single constant, modern ventilators allow a greater degree of control. In volume-cycled mode with pressure limitation, the upper pressure alarm limit is set or the maximum inspiratory pressure controlled. The ventilator delivers a preset tidal volume (V_T) unless the lungs are non-compliant or airway resistance is high. This is useful to avoid high peak airway pressures. In volume-cycled mode with a time limit, the inspiratory flow is reduced; the ventilator delivers the preset V_T unless impossible at the set respiratory rate. If pressure limitation is not available this is useful to limit peak airway pressures. In time-cycled mode with pressure control, preset pressure is delivered throughout inspiration (unlike pressure-cycled ventilation), cycling being determined by time. V_T is dependent on respiratory compliance and airway resistance. Here, too, high peak airway pressures can be avoided.

Setting up the mechanical ventilator

Tidal volume

Conventionally set at 7–10ml/kg, though recent data suggest lower values (6–7ml/kg) may be better in severe acute respiratory failure, reducing barotrauma and improving outcome. In severe airflow limitation (e.g. asthma, acute bronchitis) smaller V_T and minute volume may be needed to allow prolonged expiration.

Respiratory rate

Usually set in accordance with V_T to provide minute ventilation of 85–100ml/kg/min. In time-cycled or time-limited modes the set respiratory rate determines the timing of the ventilator cycles.

Inspiratory flow

Usually set between 40–80l/min. A higher flow rate is more comfortable for alert patients. This allows for longer expiration in patients with severe airflow limitation but may be associated with higher peak airway pressures. The flow pattern may be adjusted on most ventilators. A square waveform is often used but decelerating flow may reduce peak airway pressure.

I:E ratio

A function of respiratory rate, V_T, inspiratory flow and inspiratory time. Prolonged expiration is useful in severe airflow limitation while a prolonged inspiratory time is used in ARDS to allow slow reacting alveoli time to fill. Alert patients are more comfortable with shorter inspiratory times and high inspiratory flow rates.

FIO$_2$

Set according to arterial blood gases. Usual to start at FIO_2=0.6–1 then adjust according to arterial blood gases.

Airway pressure

In pressure-controlled or pressure-limited modes the peak airway pressure (circuit rather than alveolar pressure) can be set (usually ≤35–40cmH$_2$O). PEEP is usually increased to maintain FRC when respiratory compliance is low.

Initial ventilator set-up

Check for leaks

Check oxygen is flowing	
FIO_2	0.6–1
V_T	5–10ml/kg
Rate	10–15/min
I:E ratio	1:2
Peak pressure	≤35cmH$_2$O
PEEP	3–5cmH$_2$O

Key trial

Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000; 342:1301–8

See also:

IPPV—modes of ventilation

Controlled mechanical ventilation (CMV)

A preset number of breaths are delivered to supply all the patient's ventilatory requirements. These breaths may be at a preset V_T (volume controlled) or at a preset inspiratory pressure (pressure controlled).

Assist control mechanical ventilation (ACMV)

Patients can trigger the ventilator to determine the respiratory rate but, as with CMV, a preset number of breaths are delivered if the spontaneous respiratory rate falls below the preset level.

Intermittent mandatory ventilation (IMV)

A preset mandatory rate is set but patients are free to breathe spontaneously between set ventilator breaths. Mandatory breaths may be synchronised with patients' spontaneous efforts (SIMV) to avoid mandatory breaths occurring during a spontaneous breath. This effect, known as 'stacking' may lead to excessive tidal volumes, high airway pressure, incomplete exhalation and air trapping. Pressure support may be added to spontaneous breaths to overcome the work of breathing associated with opening the ventilator demand valve.

Pressure support ventilation (PSV)

A preset inspiratory pressure is added to the ventilator circuit during inspiration in spontaneously breathing patients. The preset pressure should be adjusted to ensure adequate V_T.

Choosing the appropriate mode

Pressure controlled ventilation avoids the dangers associated with high peak airway pressures, although it may result in marked changes in V_T if compliance alters. Allowing the patient to make some spontaneous respiratory effort may reduce sedation requirements, retrain respiratory muscles and reduce mean airway pressures.

Apnoeic patient

Use of IMV or ACMV in patients who are totally apnoeic provides the total minute volume requirement if the preset rate is high enough (this is effectively CMV) but allows spontaneous respiratory effort on recovery.

Patient taking limited spontaneous breaths

A guaranteed minimum minute volume is assured with both ACMV and IMV depending on the preset rate. The work of spontaneous breathing is reduced by supplying the preset V_T for spontaneously triggered breaths with ACMV, or by adding pressure support to spontaneous breaths with IMV. With ACMV the spontaneous tidal volume is guaranteed whereas with IMV and pressure support spontaneous tidal volume depends on lung compliance and may be less than the preset tidal volume. The advantage of IMV and pressure support is that gradual reduction of preset rate, as spontaneous effort increases, allows a smooth transition to pressure support ventilation. Subsequent weaning is by

reduction of the pressure support level.

IPPV—adjusting the ventilator

Ventilator adjustments are usually made in response to blood gases, pulse oximetry or capnography, patient agitation or discomfort, or during weaning. 'Migration' of the endotracheal tube, either distally to the carina or beyond, or proximally such that the cuff is at vocal cord level, may result in agitation, excess coughing and a deterioration in blood gases. This, and tube obstruction, should be considered and rectified before changing ventilator or sedation dose settings.

The choice of ventilator mode depends upon the level of consciousness, the number of spontaneous breaths being taken, and the blood gas values. The spontaneously breathing patient can usually cope adequately with pressure support ventilation alone. However, on occasion, a few intermittent mandatory breaths (SIMV) may be necessary to assist gas exchange or slow an excessive spontaneous rate. The paralysed or heavily sedated patient will require mandatory breaths, either volume- or pressure-controlled.

The order of change will be dictated by the severity of respiratory failure and individual operator preference. Earlier use of increased PEEP is advocated to recruit collapsed alveoli and thus improve oxygenation in severe respiratory failure.

Low PaO_2 considerations

- Increase FIO_2
- Review V_T and respiratory rate
- Increase PEEP (may raise peak airway pressure or reduce CO)
- Increase I:E ratio
- Increase pressure support/pressure control
- CMV, increase sedation ± muscle relaxants
- Consider tolerating low level ('permissive hypoxaemia')
- Prone ventilation, inhaled nitric oxide

High PaO_2 considerations

- Decrease level of pressure control/pressure support if V_T adequate
- Decrease PEEP
- Decrease FIO_2
- Decrease I:E ratio

High $PaCO_2$ considerations

- Increase V_T (if low and peak airway pressure allows)
- Increase respiratory rate
- Reduce rate if too high (to reduce intrinsic PEEP)
- Reduce dead space
- CMV, increase sedation ± muscle relaxants
- Consider tolerating high level ('permissive hypercapnia')

Low $PaCO_2$ considerations

- Decrease respiratory rate
- Decrease V_T

IPPV—failure to tolerate ventilation

Agitation or 'fighting the ventilator' may occur at any time. Poor tolerance may also be indicated by hypoxaemia, hypercapnia, ventilator alarms or cardiovascular instability.

Poor gas exchange during initial phase of ventilation

- Increase FIO_2 to 1.0 and start manual ventilation.

- Check endotracheal tube is correctly positioned and both lungs are being inflated. Consider tube replacement, intratracheal obstruction or pneumothorax.

- Check ventilator circuit is both intact and patent and ventilator is functioning correctly. Check ventilator settings including FIO_2, PEEP, I:E ratio, set tidal volume, respiratory rate and/or pressure control. Check 'pressure limit' settings as these may be set too low, causing the ventilator to time-cycle prematurely.

Poor tolerance after previous good tolerance

If agitation occurs in a patient who has previously tolerated mechanical ventilation, either the patient's condition has deteriorated or there is a problem in the ventilator circuit (including artificial airway) or the ventilator itself.

- The patient should be removed from the ventilator and placed on manual ventilation with 100% oxygen while the problem is resolved. Resorting to increased sedation ± muscle relaxation in this circumstance is dangerous until the cause is resolved.

- Check patency of the endotracheal tube (e.g. with a suction catheter) and re-intubate if in doubt.

- Consider malposition of the endotracheal tube (e.g. cuff above vocal cords, tube tip at carina, tube in main bronchus).

- Seek and treat and changes in the patient's condition, e.g. tension pneumothorax, sputum plug, pain.

- Where patients are making spontaneous respiratory effort consider increasing pressure support or adding mandatory breaths.

- If patients fail to synchronise with IMV by stacking spontaneous and mandatory breaths, increasing pressure support and reducing mandatory rate may help; alternatively, the use of PSV may be appropriate.

See also:

IPPV—complications of ventilation

Haemodynamic complications

Venous return is dependent on passive flow from central veins to right atrium. As right atrial pressure increases secondary to the transmitted increase in intrathoracic pressure across compliant lungs, there is a reduction in venous return. This is less of a problem if lungs are stiff (e.g. ARDS) although it will be exacerbated by the use of inverse I:E ratio and high PEEP. As lung volume is increased by IPPV the pulmonary vasculature is constricted, thus increasing pulmonary vascular resistance. This will increase diastolic volume of the right ventricle and, by septal shift, impedes filling of the left ventricle. These effects all contribute to a reduced stroke volume. This reduction can be minimised by reducing airway pressures, avoiding prolonged inspiratory times and maintaining blood volume.

Ventilator trauma

The term barotrauma relates to gas escape into cavities and interstitial tissues during IPPV. Barotrauma is a misnomer since it is probably the distending volume and high shear stress that is responsible rather than pressure. It is most likely to occur with high V_T and high PEEP. It occurs in IPPV and conditions associated with lung overinflation (e.g. asthma). Tension pneumothorax is life threatening and should be suspected in any patient on IPPV who becomes suddenly agitated, tachycardic, hypotensive or exhibits sudden deterioration in their blood gases. An immediate chest drainage tube should be inserted if tension pneumothorax develops. Prevention of ventilator trauma relies on avoidance of high V_T and high airway pressures.

Nosocomial infection

Endotracheal intubation bypasses normal defence mechanisms. Ciliary activity and cellular morphology in the tracheobronchial tree are altered. The requirement for endotracheal suction further increases susceptibility to infection. In addition, the normal heat and moisture exchanging mechanisms are bypassed requiring artificial humidification of inspired gases. Failure to provide adequate humidification increases the risk of sputum retention and infection. Maintaining ventilated patients at 30° upright head tilt has been shown to reduce the incidence of nosocomial pneumonia.

Acid–base disturbance

Ventilating patients with chronic respiratory failure or hyperventilation may, by rapid correction of hypercapnia, cause respiratory alkalosis. This reduces pulmonary blood flow and may contribute to hypoxaemia. A respiratory acidosis due to hypercapnia may be due to inappropriate ventilator settings or may be desired in an attempt to avoid high V_T and ventilator trauma.

Water retention

Vasopressin released from the anterior pituitary is increased due to a reduction in intrathoracic blood volume and psychological stress. Reduced urine flow thus contributes to water retention. In addition, the use of PEEP reduces lymphatic flow with consequent peripheral oedema, especially affecting the upper body. High airway pressure reduces venous return, again contributing to oedema.

Respiratory muscle wasting

Prolonged ventilation may lead to disuse atrophy of the respiratory muscles.

See also:

IPPV—weaning techniques

Patients may require all or part of their respiratory support to be provided by a mechanical ventilator. Weaning from mechanical ventilation may follow several patterns. In patients ventilated for short periods (no more than a few days) it is common to allow 20–30min breathing on a 'T' piece before removing the endotracheal tube. For patients who have received longer term ventilation it is unlikely that mechanical support can be withdrawn suddenly; several methods are commonly used to wean these patients from mechanical ventilation. There is no strong evidence that any technique is superior in terms of weaning success or rate of weaning.

Intermittent 'T' piece or continuous positive airway pressure (CPAP)

Spontaneous breathing is allowed for increasingly prolonged periods with a rest on mechanical ventilation in between. The use of a 'T' piece for longer than 30min may lead to basal atelectasis since the endotracheal tube bypasses the physiological PEEP effect of the larynx. It is therefore common to use 5cmH$_2$O CPAP as spontaneous breathing periods get longer. In the early stages of weaning, mechanical ventilation is often continued at night to encourage sleep, avoid fatigue and rest respiratory muscles.

Intermittent mandatory ventilation (IMV)

The set mandatory rate is gradually reduced as the spontaneous rate increases. Spontaneous breaths are usually pressure supported to overcome circuit and ventilator valve resistance. With this technique it is important that the patient's required minute ventilation is provided by the combination of mandatory breaths and spontaneous breaths without an excessive spontaneous rate. The reduction in mandatory rate should be slow enough to maintain adequate minute ventilation. It is also important that the patient can synchronise his own respiratory efforts with mandatory ventilator breaths; many cannot, particularly where there are frequent spontaneous breaths, some of which may 'stack' with mandatory breaths causing hyperinflation.

Pressure support ventilation

All respiratory efforts are spontaneous but positive pressure is added to each breath, the level being chosen to maintain an appropriate tidal volume. Weaning is performed by a gradual reduction of the pressure support level while the respiratory rate is <30/min. The patient is extubated or allowed to breathe with 5cmH$_2$O CPAP when pressure support is minimal (<10–15cmH$_2$O with modern ventilators).

Choice of ventilator

Modern ventilators have enhancements to aid weaning; however, weaning most patients from ventilation is possible with a basic ventilator and the intermittent 'T' piece technique, provided an adequate fresh gas flow is provided. If IMV and/or pressure support are used the ventilator should provide the features listed opposite.

Key features in the choice of ventilator

- Ventilator must allow patient triggering (i.e. not a minute volume divider)
- Fresh gas flow must be greater than spontaneous peak inspiratory flow

- Minimum circuit resistance (short, wide bore, smooth internal lumen)

- Low resistance-ventilator valves

- Sensitive pressure or flow trigger (ideally monitored close to the endotracheal tube)

- Synchronised IMV (avoids 'stacking' mandatory on spontaneous breaths)

See also:

IPPV—assessment of weaning

Assessment prior to weaning

Prior to weaning it is important that the cause of respiratory failure and any complications arising have been corrected. Sepsis should be eradicated as should other factors that increase oxygen demand. Attention is required to nutritional status and fluid and electrolyte balance. The diaphragm should be allowed to contract unhindered by choosing the optimum position for breathing (sitting up unless the diaphragm is paralysed) and ensuring that intra-abdominal pressure is not high. Adequate analgesia must be provided. Sedatives are often withdrawn by this point but may still be needed in specific situations, e.g. residual agitation, raised intracranial pressure. Weaning should start after adequate explanation has been given to the patient. Factors predicting weaning success are detailed in list opposite. Spontaneous (pressure-supported) breathing should generally start as soon as possible to allow reduction in sedation levels, and maintain respiratory muscle function. Weaning with the intention of removing mechanical support is unlikely to be successful while FIO_2 >0.4.

Assessment during weaning

Continuous pulse oximetry and regular clinical review are essential during weaning. Arterial blood gases should be taken after 20–30min of spontaneous breathing. After short term ventilation, extubate if arterial gases and respiratory pattern remain satisfactory, the cough reflex is adequate and the patient can clear sputum. Patients being weaned from longer term ventilation (>1 week) should generally be allowed to breathe spontaneously with CPAP for at least 24h before extubation.

Indications for re-ventilation

If spontaneous respiration is discoordinate or the patient is exhausted, agitated or clammy, the ventilator should be reconnected. However, clinical monitoring should avoid exhaustion. Successful weaning is more easily accomplished if excessive fatigue is not allowed to set in. Tachypnoea (>30/min), tachycardia (>110/min), respiratory acidosis (pH <7.2), rising $PaCO_2$ and hypoxaemia (SaO_2 <90%) should all prompt reconnection of the ventilator.

Factors associated with weaning failure

Failure to wean is associated with:

- Increased oxygen cost of breathing

- Muscle fatigue (hypophosphataemia, hypomagnesaemia, hypokalaemia, malnutrition, peripheral neuropathy, myopathy and drugs, e.g. muscle relaxants, aminoglycosides)

- Inadequate respiratory drive (alkalosis, opiates, sedatives, malnutrition, cerebrovascular accident, coma)

- Inadequate cardiac reserve and heart failure

In the latter case cardiac function should be monitored during spontaneous breathing periods. Any deterioration in cardiac function should be treated aggressively (e.g. optimal fluid therapy, vasodilators, inotropes).

Factors predicting weaning success

PaO_2 >11kPa on FIO_2=0.4 (PaO_2/FIO_2 ratio >27.5kPa)

Minute volume <12l/min

Vital capacity >10ml/kg

Maximum inspiratory force (PImax) >20cmH$_2$O

Respiratory rate/tidal volume <100

Qs/Qt <15%

Dead space/tidal volume <60%

Haemodynamic stability

A ratio of respiratory rate to tidal volume (f/V_T, shallow breathing index) ≤v105 has been shown to have a 78%

positive predictive value for successful weaning.

Key trial

Yang KL, Tobin MJ. A prospective study of indexes predicting the outcome of trials of weaning from mechanical ventilation. N Engl J Med 1991; 324:1445–50

See also:

IPPV—weaning techniques, p16; CO_2 monitoring, p92; Blood gas analysis, p100; Electrolytes $(Na^+, K^+, Cl^-, HCO_3^-)$, p146; Calcium, magnesium and phosphate, p148; Heart failure—assessment, p324; Acute weakness, p368; ICU neuromuscular disorders, p388

High frequency ventilation

High frequency jet ventilation (HFJV)

A high pressure jet of gas entrains further fresh gas which is directed by the jet towards the lungs. Respiratory rates of 100–300/min ensure minute volumes of about 20l/min although tidal volume may be lower than dead space. CO_2 elimination is usually more efficient than conventional IPPV. The method of gas exchange is not fully elucidated but includes turbulent gas mixing and convection. Oxygenation is dependent on mean airway pressure. Peak airway pressures are lower than with conventional mechanical ventilation but auto-PEEP and mean airway pressures are maintained. SaO_2 often falls when starting on HFJV, though usually improves with time. The high gas flow rates employed require additional humidification to be provided (30–100 ml/h); this is usually nebulised with the jet.

Indications

Bronchopleural fistula is the only proven ICU indication for HFJV though it has been used to assist weaning from mechanical ventilation as the open circuit allows spontaneous breaths without the drawbacks of demand valves. HFJV also ensures adequate ventilation if the patient fails to breathe adequately. Reducing the driving pressure and increasing the respiratory rate may facilitate weaning further. In ARDS conventional ventilation can lead to ventilator trauma if a high V_T is used. HFJV avoids problems associated with high V_T but is often unable to provide adequate ventilation in isolation for patients with severe ARDS.

Setting up HFJV

A jet must be provided via a modified endotracheal tube or catheter mount. Entrainment gas is provided via a 'T' piece. The tidal volume cannot be set directly. Rather it is set by adjusting jet size, I:E ratio, driving pressure and respiratory rate from an in-built algorithm. The respiratory rate is usually set between 100–200/min. As respiratory rate increases at a constant driving pressure the $PaCO_2$ may increase as increasing PEEPi increases the effective physiological dead space. The I:E ratio is usually set between 1:3 and 1:2. V_T is determined by airway pressure and I:E ratio. Driving pressure is usually set between 1–2bar. These pressures are much higher than the 60–100cmH$_2$O used in conventional ventilation. PEEPi is related to the driving pressure, I:E ratio and respiratory rate. External PEEP may be added to increase mean airway pressure should this be necessary to improve oxygenation.

Combined HFJV and conventional CMV

May be useful in ARDS where HFJV alone cannot provide adequate gas exchange. Low frequency pressure limited ventilation with PEEP provides an adequate mean airway pressure to ensure oxygenation while CO_2 clearance is effected by HFJV. Care must be taken to avoid excessive peak airway pressure when HFJV and CMV breaths stack.

High frequency oscillation (HFO)

This technique can be applied externally (see 'Non-invasive respiratory support') or via the endotracheal tube. In the latter instance high rates are applied and the driving pressure gradually increased. The FRC increases, recruiting alveoli and improving oxygenation. The airway pressure can then be wound down, often without any significant deterioration in oxygenation.

Adjusting HFJV according to blood gases

Increasing PaO$_2$

Increase FIO$_2$

Increase I:E ratio

Increase driving pressure

Add external PEEP

Consider reducing respiratory rate

Decreasing PaCO$_2$

Increase driving pressure

Decrease respiratory rate

Positive end expiratory pressure (1)

Positive end expiratory pressure (PEEP) is a modality used in positive pressure ventilation to prevent the alveoli returning to atmospheric pressure during expiration. It is routinely set between 3–5cmH$_2$O; however, in severe respiratory failure it will often need to exceed 10cmH$_2$O to be above the lower inflexion point of the pressure–volume curve. This has been suggested as beneficial in patients with severe ARDS. It rarely needs to exceed 20cmH$_2$O to avoid cardiorespiratory complications and alveolar over-distension (see below). It does not prevent nor attenuate ARDS, or reduce capillary leak or lung water.

Respiratory effects

PEEP improves oxygenation by recruiting collapsed alveoli, redistributing lung water, decreasing A–V mismatch and increasing FRC.

Haemodynamics

PEEP usually lowers both left and right ventricular preload and increases RV afterload. Though PEEP may increase cardiac output in left heart failure and fluid overload states by preload reduction, in most other cases cardiac output falls, even at relatively low PEEP levels. PEEP may also compromise a poorly functioning right ventricle. Improved PaO$_2$ resulting from decreased venous admixture may sometimes arise solely from reductions in cardiac output.

Physiological PEEP

A small degree of PEEP (2–3cmH$_2$O) is usually provided physiologically by a closed larynx. It is lost when the patient is intubated or tracheostomised and breathing spontaneously on a 'T' piece with no CPAP valve (see CPAP).

Intrinsic PEEP (auto-PEEP, air trapping, PEEPi)

Increased level of PEEP due to insufficient time for expiration, leading to 'air trapping', CO$_2$ retention, increased airway pressures and increased FRC. Seen in pathological conditions of increased airflow resistance (e.g. asthma, emphysema) and when insufficient expiratory time is set on the ventilator. Used clinically in inverse ratio ventilation to increase oxygenation and decrease peak airway pressures. High levels of PEEPi can, however, slow weaning by an increased work of breathing; use of extrinsic PEEP may overcome this. PEEPi can be measured by temporarily occluding the expiratory outlet of ventilator at end-expiration for a few seconds to allow equilibration of pressure between upper and lower airway and then reading the ventilator pressure gauge (or print-out).

'Best' PEEP

Initially described as the level of PEEP producing the lowest shunt value. Now generally considered to be the lowest level of PEEP that achieves SaO$_2 \geq 90\%$ allowing, wherever possible, lowering of FIO$_2$ (ideally ≤ 0.6) though not at the expense of peak airway pressures >35–40cmH$_2$O or significant reductions in DO$_2$.

Positive end expiratory pressure (2)

Adjusting PEEP

1. Measure blood gases and monitored haemodynamic variables.

2. If indicated, alter level of PEEP by 3–5cmH$_2$O increments.

3. Re-measure gases and haemodynamic variables after 15–20min.

4. Consider further changes as necessary (including additional changes in PEEP, fluid challenge or vasoactive drugs).

A number of clinical trials have adjusted PEEP levels according to FIO$_2$ requirements (see table). Although unlikely to constitute 'optimal PEEP' for an individual patient, this provides a useful approximation and starting point for further titration of therapy.

FIO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP (cmH_2O)	5	5	8	8	10	10	10	12	14	14	14	16	18	≥18

Indications

- Hypoxaemia requiring high FIO_2
- Optimisation of pressure–volume curve in severe respiratory failure
- Hypoxaemia secondary to left heart failure
- Improvement of cardiac output in left heart failure
- Reduced work of breathing during weaning in patients with high PEEPi
- Neurogenic pulmonary oedema (i.e. non-cardiogenic pulmonary oedema following relief of upper airway obstruction)

Complications

- Reduced cardiac output. May need additional fluid loading or even inotropes. This should generally be avoided unless higher PEEP is necessary to maintain adequate arterial oxygenation. Caution should be exercised in patients with myocardial ischaemia.
- Increased airway pressure (and potential risk of ventilator trauma).
- Overinflation leading to air trapping and raised $PaCO_2$. Use with caution in patients with chronic airflow limitation or asthma. In pressure- controlled ventilation overdistension is suggested when an increase in PEEP produces a significant fall in tidal volume.
- High levels will decrease venous return, raise intracranial pressure and increase hepatic congestion.
- PEEP may change the area of lung in which a pulmonary artery catheter tip is positioned from West Zone III to non-Zone III. This is suggested by a rise in wedge pressure of at least half the increase in PEEP and requires resiting of the PA catheter.

See also:

Continuous positive airway pressure

Continuous positive airway pressure (CPAP) is the addition of positive pressure to the expiratory side of the breathing circuit of a spontaneously ventilating patient who may or may not be intubated. This sets the baseline upper airway pressure above atmospheric pressure, prevents alveolar collapse and possibly recruits already collapsed alveoli. It is usually administered in increments of 2.5cmH$_2$O to a maximum of 10cmH$_2$O and applied via either a tight-fitting face mask (face CPAP), nasal mask (nasal CPAP) or expiratory limb of a 'T' piece breathing circuit. A high flow (i.e. above peak inspiratory flow) inspired air-oxygen supply, or a large reservoir bag in the inspiratory circuit, is necessary to keep the valve open. CPAP improves oxygenation and may reduce the work of breathing by reducing the alveolar-to-mouth pressure gradient in patients with high levels of intrinsic PEEP. Transient periods of high CPAP (e.g. 40cm H$_2$O for 40s) may be a useful manoeuvre for recruiting collapsed alveoli and improving oxygenation in ARDS.

Indications

- Hypoxaemia requiring high respiratory rate, effort and FIO_2.
- Left heart failure to improve hypoxaemia and cardiac output.
- Weaning modality.
- Reducing work of breathing in patients with high PEEPi (e.g. asthma, chronic airflow limitation). NB: use with caution and monitor closely.

Complications

- With mask CPAP there is an increased risk of aspiration as gastric dilatation may occur from swallowed air. Insert nasogastric tube, especially if consciousness is impaired or gastric motility is reduced.

- Reduced cardiac output due to reduced venous return (raised intra-thoracic pressure). May need additional fluid or even inotropes.

- Overinflation leading to air trapping and high $PaCO_2$. Caution is urged in patients with chronic airflow limitation or asthma.

- High levels will reduce venous return and increase intracranial pressure.

- Occasional poor patient compliance with tight-fitting face mask due to feelings of claustrophobia and discomfort on bridge of nose.

- Inspissated secretions due to high flow, dry gas.

Management

1. Measure blood gases, monitor haemodynamic variables and respiratory rate.

2. Prepare 'T' piece circuit with a $5cmH_2O$ CPAP valve on the expiratory limb. Connect inspiratory limb to flow generator/large volume reservoir bag. Adjust air-oxygen mix to obtain desired FIO_2 (measured by oxygen analyser in circuit). Use a heat–moisture exchanger to humidify the inhaled gas. If not intubated, consider either nasal or face CPAP. Attach mask to face by appropriate harness and attach 'T'piece to mask. Ensure no air leak around mask. If using a nasal mask, encourage the patient to keep their mouth closed.

3. Measure gases, respiratory rate, and haemodynamics after 15–20min.

4. Consider further changes in CPAP (by $2.5cmH_2O$ increments)

5. Consider need for (i) fluid challenge (or vasoactive drugs) if circulatory compromise and (ii) nasogastric tube if gastric atony present.

See also:

Lung recruitment

There has been considerable interest in recent years in the concept of lung recruitment. The rationale is that reopening of collapsed alveoli will result in improved gas exchange, with resulting reductions in airway pressures and FIO_2. Timing is crucial as collapsed alveoli are more likely to be recruitable in the early stages of respiratory failure.

It appears that benefit is more likely in non-respiratory causes of ARDS, rather than in cases of direct pulmonary pathology such as pneumonia. Some animal studies suggest that recruitment procedures may even be potentially injurious in the latter situation.

Consideration should be given to lung recruitment soon after intuba-tion in patients with severe respiratory failure, and procedures causing de-recruitment, e.g. endotracheal suction and airway disconnection.

Recruitment techniques

A number of techniques are described to recruit collapsed alveoli, such as applying $40cmH_2O$ PEEP for 40s with no ventilator breaths; delivering a few large-volume, ventilator-delivered breaths; or by using a combination of varying levels of PEEP and increasing pressure-delivered breaths to obtain optimal gas exchange.

Although anecdotal successes are reported, with occasionally dramatic improvements in lung compliance and gas exchange, no comparative trials have been performed, and outcomes have not been assessed prospectively. Haemodynamic compromise may occur during the procedure, though this usually recovers on cessation.

Key trial

Brower RG, et al for the ARDS Clinical Trials Network. Effects of recruitment maneuvers in patients with acute lung injury and acute respiratory distress syndrome ventilated with high positive end-expiratory pressure. Crit Care Med 2003; 31:2592–7

Prone positioning

Prone positioning is used to treat patients with acute respiratory distress syndrome (ARDS) to improve gas exchange.

A number of theories have been proposed to explain why the prone position helps. These theories include: reduction in compression atelectasis of dependent lung regions (temporary), reduction in chest wall compliance increasing intrathoracic pressure and alveolar recruitment, better regional diaphragmatic movement, better V/Q matching, improved secretion clearance and less alveolar distension leading to better oxygenation.

Indications

Prone positioning may be considered when: PaO_2 <8.5kPa, $FIO_2 \geq 0.6$, PEEP >10cmH$_2$O despite optimisation of other ventilatory support.

Technique

Positioning the patient takes time and preparation. Four members of staff are required to turn the patient and one person to secure the head and endotracheal tube. The turn itself is a two-stage procedure via the lateral position. The arm on which the patient is to be rolled is tucked under the hip with the other arm laid across the chest. Pillows are placed under the abdomen and chest prior to rotation to the lateral position. If stable, turn may be completed to prone. Pillows are placed under the shoulders and pelvis. The head of the bed is raised and one arm is extended at the patient's side while the other is flexed with the head facing the opposite way.

Frequency of turns

The response to prone ventilation is difficult to predict. Some patients may have no improvement in gas exchange; others may have a temporary benefit, requiring frequent turns, and others may have difficulty returning to a supine position. For compression atelectasis it is likely that benefit will last up to 2h before resumption of a supine position is required. For other conditions, up to 18h prone positioning may be required. The head and arms should be repositioned 2-hrly.

Complications

There are problems associated with positioning the patient prone including: facial oedema, incorrect positioning of limbs leading to nerve palsy and accidental removal of drains and catheters, pressure necrosis, myositis ossificans. These problems are preventable provided there is awareness of their potential.

Contraindications

There are two absolute contraindications to prone position: severe head, spinal or abdominal injury and severe haemodynamic instability. Relative contraindications include:

- Recent abdominal surgery
- Large abdomen
- Pregnancy
- Spinal instability (though special beds are available for turning affected patients)
- Frequent seizures
- Multiple trauma
- Raised ICP

Key trial

Gattinoni L, et al for the Prone-Supine Study Group. Effect of prone positioning on the survival of patients with acute respiratory failure. N Engl J Med 2001; 345:568–73

See also:

Acute respiratory distress syndrome (1), p292; Acute respiratory distress syndrome (2), p294

Non-invasive respiratory support

Devices of varying sophistication are available to augment spontaneous breathing in the compliant patient by either assisting inspiration (inspiratory support) and/or providing CPAP. Non-invasive support is usually delivered by tight fitting face or nasal mask, though a helmet may be used and inspiratory support can be delivered by mouthpiece. Some devices allow connection to an endotracheal tube for the intubated but spontaneously breathing patient.

Indications

- Hypoxaemia requiring high respiratory rate, effort and FIO_2
- Hypercapnia in a fatiguing patient
- Weaning modality
- To avoid endotracheal intubation where desirable (e.g. severe chronic airflow limitation, immunosuppressed patients)
- Reduces work of breathing in patients with high PEEPi (e.g. asthma, chronic airflow limitation). Use with caution

and monitor closely

- Physiotherapy technique for improving FRC

- Sleep apnoea

Inspiratory support (IS)

A preset inspiratory pressure is given which is triggered by the patient's breath. This trigger can be adjusted according to the degree of patient effort. Some devices will deliver breaths automatically at adjustable rates and the I:E ratio may also be adjustable. The tidal volume delivered for a given level of inspiratory support will vary according to the patient's respiratory compliance. An example of an IS device is the Bird ventilator commonly used by physiotherapists for improving FRC and expanding lung bases.

BiPAP (Bi-level Positive Airways Pressure)

This device delivers adjustable levels of pressure support and PEEP. Delivered breaths can be either patient-triggered and/or mandatory. Some BiPAP devices are driven by air; to increase the FIO_2, supplemental oxygen can be given via a circuit connection or through a portal in the mask.

Management

1. Select type and delivery mode of ventilatory support.

2. Connect patient as per device instructions.

3. Use an appropriate sized mask that is comfortable and leak-free.

4. A delivered pressure of 10–15cmH$_2$O is a usual starting point which can be adjusted according to patient response (respiratory rate, degree of fatigue, comfort, blood gases…).

5. Expiratory pressure support levels are usually within the 5–12cmH$_2$O range.

6. Patients in respiratory distress may have initial difficulty in coping with these devices. Constant attention and encouragement help to accustom the patient to the device and/or mask while different levels of support, I:E ratios etc. are being tested to find the optimal setting. Cautious administration of low dose subcutaneous opiate injections (e.g. diamorphine 2.5mg) may help to calm the patient without depressing respiratory drive. The tight-fitting mask may be found increasingly claustrophobic after a few days' use. This should be pre-empted if possible by allowing the patient regular breaks. Pressure areas such as the bridge of the nose should be protected.

Key trials

Brochard L, et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. N Engl J Med 1995; 333:817–22

Antonelli M, et al. A comparison of noninvasive positive-pressure ventilation and conventional mechanical ventilation in patients with acute respiratory failure. N Engl J Med 1998; 339:429–35

Extracorporeal respiratory support

These techniques have declined in popularity over recent years after several trials failed to demonstrate clear outcome benefit in adults with very severe respiratory failure. Survival rates of 50–60% are reported but clear superiority over conventional ventilation has not yet been demonstrated in controlled studies. A large prospective randomised study (the 'CESAR' trial) is currently under way in the UK.

Extracorporeal CO$_2$ removal (ECCO$_2$R)

An extracorporeal veno-venous circulation allows CO_2 clearance via a gas exchange membrane. Blood flows of 25–33% cardiac output are typically used which only allow for partial oxygenation support. Low frequency (4–5/min) positive pressure ventilation is usually used with ECCO$_2$R with continuous oxygenation throughout inspiration and expiration. The lungs are 'held open' with high PEEP (20–25cmH$_2$O), limited peak airway pressures (35–40cmH$_2$O) and a continuous fresh gas supply. Thus, oxygenation is effected with lung rest to aid recovery. Anticoagulation of the extracorporeal circuit can be reduced by using heparin-bonded tubing and membranes.

Extracorporeal membrane oxygenation (ECMO)

An extracorporeal veno-arterial circulation with high blood flows (approaching cardiac output) through a gas exchange membrane enables most if not all of the body's gas exchange requirements to be met. The main disadvantages compared to ECCO$_2$R are the need for large bore arterial puncture with its consequent risks, and high extracorporeal blood flows with the potential for cell damage.

Indications

Failure of maximum intensive therapy and ventilatory support to sustain adequate gas exchange as evidenced by the criteria below.

Contraindications

- Chronic systemic disease involving any major organ system (e.g. irreversible chronic CNS disease, chronic lung disease with FEV_1 <1l, FEV_1/FVC <0.3 of predicted, chronic $PaCO_2$ >6.0kPa, emphysema or previous admission for chronic respiratory insufficiency, incurable or rapidly fatal malignancy, chronic left heart failure, chronic renal failure, chronic liver failure, HIV related disease).

- Lung failure for >7 days (although treatment with extracorporeal respiratory support may persist for longer than 14 days).

- Burns (>40% of body surface).

- More than 3 organ failures in addition to lung failure.

Criteria for $ECCO_2R/ECMO$

i. Rapid failure of ventilatory support: immediate use of these techniques should be considered in those meeting the following criteria for a period >2h despite maximum intensive care:

PaO_2 <6.7kPa

FIO_2 1.0

PEEP >5cmH$_2$O

ii. Slow failure of ventilatory support: consider use after 48h maximum intensive care for those meeting the following gas exchange and mechanical pulmonary function criteria for a period >12h:

PaO_2 <6.7kPa	PEEP >5cmH$_2$O
Qs/Qt >30% on FIO_2 = 1.0	FIO_2 >0.6
PaO_2/FIO_2 <11.2kPa	TSLC <30ml/cmH$_2$O at 10ml/kg inflation

See also:

Anticoagulants, p248; Prostaglandins, p264; Acute respiratory distress syndrome (1), p292; Acute respiratory distress syndrome (2), p294

Endotracheal intubation

Indications

An artificial airway is necessary in the following circumstances:

- Apnoea—Provision of mechanical ventilation, e.g. unconsciousness, severe respiratory muscle weakness, self-poisoning

- Respiratory failure—Provision of mechanical ventilation, e.g. ARDS, pneumonia

- Airway protection—Unconsciousness, trauma, aspiration risk, poisoning

- Airway obstruction—Maintain airway patency, e.g. trauma, laryngeal oedema, tumour, burns

- Haemodynamic instability—Facilitate mechanical ventilation, e.g. shock, cardiac arrest

Choice of endotracheal tube

Most adults require a standard high volume, low pressure cuffed endotracheal tube. The average sized adult will require a size 8.0–9.0mm id tube (size 7.5–8.0mm id for females) cut to a length of 23cm (21cm for females). Particular problems with the upper airway, e.g. trauma, oedema, may require a smaller tube. In specific situations non-standard tubes may be used, e.g. jet ventilation, armoured tubes to avoid external compression and double lumen tubes to isolate the right or left lung.

Route of intubation

The usual routes of intubation are oro-tracheal and naso-tracheal. Oro-tracheal intubation is preferred. The naso-tracheal route has the advantages of increased patient comfort and the possibility of easier blind placement; it is also easier to secure the tube. However, there are several disadvantages. The tube is usually smaller, there is a risk of sinusitis and otitis media and the route is contraindicated with concurrent coagulopathy, CSF leak and nasal fractures.

Difficult intubation

If a difficult intubation is predicted, it should not be attempted by an inexperienced operator. Difficulty may be predicted in the patient with a small mouth, high arched palate, large upper incisors, hypognathia, large tongue, anterior larynx, short neck, immobile temporo-mandibular joints, immobile cervical joints or morbid obesity. If a difficult intubation presents unexpectedly, the use of a stylet, a straight bladed laryngoscope or a fibreoptic laryngoscope may help. It is important not to persist for too long; revert to bag and mask ventilation to ensure adequate oxygenation.

Complications of intubation

Early complications

- Trauma, e.g. haemorrhage, mediastinal perforation
- Haemodynamic collapse, e.g. positive pressure ventilation, vasodilatation, arrhythmias or rapid correction of hypercapnia
- Tube malposition, e.g. failed intubation or endobronchial intubation

Later complications

- Infection including maxillary sinusitis if nasally intubated
- Cuff pressure trauma (avoid by maintaining cuff pressure <25cmH$_2$O)
- Mouth/lip trauma

Equipment required

Suction (Yankauer tip)

Oxygen supply, rebreathing bag and mask

Laryngoscope (two curved blades and straight blade)

Stylet/bougie

Endotracheal tubes (preferred size and smaller)

Magill forceps

Drugs (induction agent, muscle relaxant, sedative)

Syringe for cuff inflation

Tape to secure tube

Capnograph

See also:

Tracheotomy

Indications

To provide an artificial airway in place of oro- or naso-tracheal intubation. This may be to provide better patient comfort, to avoid vocal cord, mouth or nasal trauma or, in an emergency, to bypass acute upper airway obstruction. The optimal time to perform a tracheotomy in an intubated patient is not known; current practice suggests 10–16 days, or sooner if prolonged intubation is predicted, especially in cases of difficult intubation. Avoiding the risks of vocal cord damage may provide some advantage for a tracheostomy. The reduced need for sedation, the potential to eat, drink and speak and the facilitation of mouth care are all definite advantages.

Percutaneous tracheotomy

A more rapid procedure with less tissue trauma and scarring than the standard open surgical technique. It can be performed in the ICU, avoiding the need to transfer patients to theatre. Coagulopathy should be excluded or treated first. Subcutaneous tissues are infiltrated with 1% lidocaine and epinephrine (adrenaline). After a 1–1.5cm midline skin crease incision, the subcutaneous tissue is blunt dissected to the anterior tracheal wall. The endotracheal tube tip is withdrawn to the level of the vocal cords. The trachea is then punctured in the midline with a 14G needle between the 1st and 2nd tracheal cartilages (or lower), allowing guide wire insertion. The stoma is created by dilatation to 32–36Fr (Ciaglia technique) or by a guided forceps dilating tool (Schachner–Ovill technique). In the former case, the tracheostomy tube is introduced over an appropriate sized dilator and in the latter through the open

dilating tool. End-tidal CO_2 monitoring confirms adequate ventilation during the procedure. Fibreoptic bronchoscopy may be used to confirm correct tracheal placement and no trauma to the posterior tracheal wall, though this may compromise ventilation.

Complications

The main early complication is haemorrhage from vessels anterior to the trachea. This is usually controlled with direct pressure or, occasionally, sutures. Bleeding into the trachea may result in clot obstruction of the airway; endotracheal suction is usually effective. Paratracheal placement should be rare but promptly recognised by inability to ventilate the lungs. Later complications include tracheostomy displacement, stomal infection and tracheal stenosis. Stenosis is often related to low grade infection and is claimed to be more common with open tracheotomy. Rare complications include tracheo-oesophageal fistula due to trauma or pressure necrosis of the posterior tracheal wall, or erosion through the lateral tracheal wall into a blood vessel.

Maintenance of a tracheotomy

Since the upper air passages have been bypassed, artificial humidification is required. Cough is less effective without a functioning larynx so regular tracheal suction will be necessary. Furthermore, the larynx provides a small amount of natural PEEP that is lost with a tracheostomy. The risk of basal atelectasis can be overcome with CPAP or attention to respiratory exercises that promote deep breathing. A safe fistula forms within 3–5 days, allowing replacement of the tracheotomy tube.

Tracheotomy tubes

Standard high volume, low pressure cuff

Fenestrated with or without cuff

Useful where airway protection is not a primary concern. May be closed during normal breathing while providing intermittent suction access.

Fenestrated with inner tube

As above but with an inner tube to facilitate closure of the fenestration during intermittent mechanical ventilation.

Fenestrated with speaking valve

Inspiration allowed through the tracheostomy to reduce dead space and inspiratory resistance. Expiration through the larynx, via the fenestration, allowing speech and the advantages of laryngeal PEEP.

Adjustable flange

Accommodates extreme variations in skin to trachea depth while ensuring the cuff remains central in the trachea.

Pitt speaking tube

A non-fenestrated, cuffed tube for continuous mechanical ventilation and airway protection with a port to direct airflow above the cuff to the larynx. When airflow is directed through the larynx some patients are able to vocalise.

Passy–Muir speaking valve

This is an expiratory occlusive valve placed onto the tracheostomy tube that permits inspiration through the tracheostomy and expiration through the glottis. The tracheostomy tube cuff must be first deflated. The valve allows phonation, facilitates swallowing and may reduce aspiration. Small studies have suggested that it may reduce the work of breathing. The potential tidal volume drop through cuff deflation makes this valve only suitable in those patients requiring no (or relatively low level) invasive ventilatory support.

Silver tube

An uncuffed tube used occasionally in ENT practice to maintain a tracheostomy fistula.

See also:

Ventilatory support—indications, p4; Opioid analgesics, p234; Sedatives, p238; Muscle relaxants, p240; Cardiac arrest, p272; Airway obstruction, p280; Respiratory failure, p282; Acute chest infection (1), p288; Acute chest infection (2), p290; Acute respiratory distress syndrome (1), p292; Acute respiratory distress syndrome (2), p294; Asthma—general management, p296; Asthma—ventilatory management, p298; Poisoning—general principles, p452. Post-operative intensive care, p534

Minitracheotomy

A 4mm diameter uncuffed plastic tube inserted through the cricothyroid membrane under local anaesthetic.

Indications

- Removal of retained secretions, usually if patient's cough is weak
- Emergency access to lower airway if upper airway obstructed

Contraindications/cautions

- Coagulopathy
- Non-compliant, agitated patient (unless sedated)

Technique

Some commercial kits rely on blind insertion of a blunt introducer; others use a Seldinger technique where a guidewire is inserted via the cricothyroid membrane into the trachea. An introducer passed over the wire dilates the track allowing easy passage of the tube.

1. Use aseptic technique. Cleanse site with antiseptic. Locate cricothyroid membrane (midline 'spongy' area between cricoid and thyroid cartilages).

2. Infiltrate local skin and subcutaneous tissues with 1% lidocaine ± epinephrine (adrenaline). Advance needle into deeper tissues, aspirating to confirm absence of blood then infiltrating with lidocaine until cricothyroid membrane is pierced and air can be easily aspirated.

3. (If using Seldinger technique insert guidewire through membrane into trachea.) Tether thyroid cartilage with one hand, incise skin and tissues vertically in midline (alongside wire) with short-bladed guarded scalpel provided with pack. Insert scalpel to blade guard level to make adequate hole through cricothyroid membrane. Remove scalpel.

4. Insert blunt introducer through incision site into trachea (or over guidewire). Angle caudally. Relatively light resistance will be felt during correct passage—do not force introducer if resistance proves excessive.

5. Lubricate plastic tube with gel. Slide tube over introducer into trachea.

6. Remove introducer (+ wire), leaving plastic tube *in situ*.

7. Confirm correct position by placing own hand over tube and feeling airflow during breathing. Suction down tube to aspirate intratracheal contents (check pH if in doubt). Cap opening of tube. Suture to skin.

8. Perform CXR (unless very smooth insertion and no change in cardio-respiratory variables).

9. O_2 can be entrained through the tube, or an appropriate connector (provided in pack) placed to allow bagging, use of the Bird ventilator and/or short term assisted ventilation.

Complications

- Puncture of blood vessel at cricothyroid membrane may cause significant intratracheal or external bleeding. Apply local pressure if this occurs after blade incision. If bleeding continues, insert minitracheotomy tube for a tamponading effect. If bleeding persists, insert deep sutures either side of minitracheotomy; if this fails, contact surgeon for assistance
- Perforation of oesophagus
- Mediastinitis (rare)
- Pneumothorax

See also:

Chest drain insertion

Indications

Drainage of air (pneumothorax), fluid (effusion), blood (haemothorax) or pus (empyema) from the pleural space.

Insertion technique

1. Use 28Fr drain (or larger) for haemothorax or empyema; 20Fr will suffice for a pure pneumothorax. Seldinger-type drains with an integral guidewire are now also available. The drain is usually inserted through the 5th intercostal space in the mid-axillary line, first anaesthetising skin and pleura with 1% lidocaine. Ensure that air/fluid/blood/pus is aspirated.

2. Make a 1–1.5cm skin crease incision, create a track with gloved finger (or forceps) to separate muscle fibres and open pleura.

3. Insert drain through open pleura with trochar withdrawn to ensure tip is blunt to avoid lung damage. Angle and insert drain to correct position (towards lung apex for a pneumothorax and lung base for a haemothorax/effusion). Connect drain to the underwater seal. CT scan or ultrasound may be useful for directing placement for focal/small collections.

4. Secure drain to chest wall by properly placed sutures.

5. Perform CXR to ensure correct siting and lung reinflation.

6. Place on 5–10cmH$_2$O (0.5–1.3kPa) negative pressure (low pressure wall suction) if lung has not fully expanded.

Subsequent management

- Drains should not be clamped prior to removal, or transport of patient.

- Drains may be removed when the lung has re-expanded and there is no air leak (no respiratory swing in fluid level or air leak on coughing).

- Unless long term ventilation is necessary, a drain inserted for a pneumothorax should usually be left *in situ* during IPPV.

- Remove drain at end-expiration. Cover hole with thick gauze and Elastoplast; a purse-string suture is not usually necessary. Repeat CXR if indicated by deteriorating clinical signs or blood gas analysis.

Complications

- Morbidity associated with chest drainage may be up to 10%.

- Puncture of intercostal vessel may cause significant bleeding. Consider (i) correcting any coagulopathy, (ii) placing deep tension sutures around drain or (iii) removing drain, inserting a Foley catheter, inflating the balloon and applying traction to tamponade bleeding vessel. If these measures fail, contact (thoracic) surgeon.

- Puncture of lung tissue may cause a bronchopleural fistula. If chest drain suction (up to 15–20cmH$_2$O) fails, consider (i) pleurodesis (e.g. with tetracycline), (ii) high frequency jet ventilation ± double-lumen endobronchial tube, or (iii) surgery. Extubate if feasible.

- Perforation of major vessel (often fatal)—clamp but do not remove drain, resuscitate with blood, contact surgeon, consider double-lumen endotracheal tube.

- Infection—take cultures; antibiotics (staphylococcal ± anaerobic cover); consider removing/resiting drain.

- Local discomfort/pain from pleural irritation may impair cough. Consider simple analgesia, subcutaneous lidocaine, instilling local anaesthetic, local or regional anaesthesia, etc.

- Drain dislodgement—if needed, replace/resite new drain, depending on cleanliness of site. Don't advance old drain (infection risk).

- Lung entrapment/infarction—avoid milking drain in pneumothorax.

See also:

Pleural aspiration
Drainage of fluid from the pleural space using either a needle, cannula or flexible small-bore drain. Increasingly being performed under ultrasound guidance. Blood/pus usually requires large-bore drain insertion.

Indications

- Improvement of blood gases

- Symptomatic improvement of dyspnoea

- Diagnostic 'tap'

Contraindications/Cautions

- Coagulopathy

Complications

- Puncture of lung or subdiaphragmatic viscera

- Bleeding

Fluid protein level
Protein >30g/l (this should be viewed in the context of the plasma protein level)-exudate—causes: inflammatory e.g. pneumonia, pulmonary embolus, neoplasm, collagen vascular diseases

Protein <30g/l-transudate—causes: (i) increased venous pressure (e.g. heart failure, fluid overload), (ii) decreased colloid osmotic pressure (e.g. critical illness leading to reduced plasma protein from capillary leak and hepatic dysfunction, hepatic failure, nephrotic syndrome)

Technique

1. Confirm presence of effusion by CXR or ultrasound.

2. Select drainage site either by maximum area of stony dullness under percussion or under ultrasound guidance.

3. Use aseptic technique. Clean area with antiseptic and infiltrate local skin and subcutaneous tissues with 1% lidocaine. Advance into deeper tissues, aspirating to confirm absence of blood then infiltrating with local anaesthetic until pleura is pierced and fluid can be aspirated.

4. Advance drainage needle/cannula/drain slowly, applying gentle suction, through chest wall and intercostal space (above upper border of rib to avoid neurovascular bundle) until fluid can be aspirated.

5. Withdraw 50ml for microbiological (M, C&S, TB stain, etc.), biochemical (protein, glucose, etc.) and histological/cytological (pneumocystis, malignant cells, etc.) analysis as indicated.

6. Either leave drain *in situ* connected to drainage bag or connect needle/cannula by 3-way tap to drainage apparatus.

7. Continue aspiration/drainage until no further fluid can be withdrawn or if patient becomes symptomatic (pain/dyspnoea). Dyspnoea or haemodynamic changes may occur due to removal of large volumes of fluid (>1–2l) and subsequent fluid shifts; if this is considered to be a possibility, remove no more than 1l at a time either by clamping/declamping drain or repeating needle aspiration after an equilibration interval (e.g. 4–6h).

8. Remove needle/drain. Cover puncture site with firmly applied gauze dressing.

See also:

Fibreoptic bronchoscopy

Indications

Diagnostic

- Collection of microbiological ± cytological specimens (by broncho- alveolar lavage, protected brush specimen, biopsy).

- Cause of bronchial obstruction (e.g. clot, foreign body, neoplasm).

- Extent of inhalation injury.

- Diagnosis of ruptured trachea/bronchus.

Therapeutic

- Clearance of secretions, inhaled vomitus, etc.

- Removal of lumen-obstructing matter (e.g. mucus plug, blood clot, food, tooth). Proximal obstruction rather than consolidation is suggested by the radiological appearance of a collapsed lung/lobe and no air bronchogram.

- Cleansing—removing soot or other toxic materials, irrigation with saline.

- Directed physiotherapy ± saline to loosen secretions.

- Directed placement of balloon catheter to arrest pulmonary bleeding.

- To aid difficult endotracheal intubation.

Contraindications/cautions

- Coagulopathy
- Severe hypoxaemia

Complications

- Hypoxaemia—from suction, loss of PEEP, partial obstruction of endotracheal tube and non-delivery of tidal volume.

- Haemodynamic disturbance including hypertension and tachycardia (related to hypoxaemia, agitation, tracheal stimulation, etc.).
- Bleeding.
- Perforation (unusual though more common if biopsy taken).

Procedure

It is difficult to perform fibreoptic bronchoscopy in a nasally intubated patient. A narrow-lumen scope can be used but suction is limited.

1. Pre-oxygenate with FIO_2 1.0. Monitor with pulse oximetry.
2. Increase pressure alarm limit on ventilator.
3. Lubricate scope with lubricant gel/saline.
4. If unintubated, apply lidocaine gel to nares ± spray to pharynx.
5. Consider short-term IV sedation ± paralysis.
6. Insert scope nasally (in a non-intubated patient) or through catheter mount port in an intubated patient. An assistant should support the endotracheal tube during the procedure to minimise trauma to both trachea and scope.
7. Inject 2% lidocaine into trachea to prevent coughing and haemodynamic effects from tracheal/carinal stimulation.
8. Perform thorough inspection and any necessary procedures. If SpO_2 ≤85% or haemodynamic disturbance occurs, remove scope and allow re-oxygenation before continuing.
9. Bronchoalveolar lavage is performed by instillation of at least 60ml of (preferably warm) isotonic saline into affected lung area without suction, followed by aspiration into a sterile catheter trap. All bronchoscopic samples should be sent promptly to the lab.
10. Reduction of effective endotracheal tube lumen and suction may affect the tidal volume, leading to hypoxaemia and/or hypercapnia.
11. After procedure, reset ventilator as appropriate.

Chest physiotherapy

The aim is to expand collapsed alveoli, mobilise chest secretions or re-inflate collapsed lung segments. No scientific validation of effectiveness has been reported. The current view is that routine 'prophylactic' suctioning/ bagging should be avoided in the critically ill.

Indications

- Mobilisation of secretions.
- Re-expansion of collapsed lung/lobes.
- Prophylaxis against alveolar collapse and secondary infection.

Contraindications/cautions

- Aggressive hyperinflation in already hyperinflated lungs, e.g. asthma, emphysema—though can be very useful in removing mucus plugs.
- Undrained pneumothorax.
- Raised intracranial pressure.

Techniques

Hyperinflation

Hyperinflating to 50% above ventilator-delivered V_T, aiming to expand collapsed alveoli and mobilise secretions. V_T is rarely measured, so either excessive or inadequate hyperinflations may be given depending on lung compliance and operator technique. Pressure-limiting devices ('blow-off valves') or manometers can avoid excessive airway pressures. A recommended technique is slow inspiration, a 1–2s plateau phase and then rapid release of the bag to simulate a 'huff' and mobilise secretions. Pre-oxygenation may be needed as PEEP may be lost and the delivered V_T may be inadequate. Cardiac output often falls with variable blood pressure and heart rate responses. Sedation may blunt the haemodynamic response. Full deflation avoids air trapping.

Suction

Removing secretions from trachea and main bronchi (usually right). A cough reflex may be stimulated to mobilise

secretions further. Tenacious secretions may be loosened by instillation of 2–5 ml 0.9% saline. Falls in SaO_2 and cardiovascular disturbance may be avoided by pre-oxygenation.

Percussion and vibration
Drumming and shaking actions over chest wall to mobilise secretions.

Inspiratory pressure support (Bird ventilator)
The aim is to increase FRC and expand collapsed alveoli.

Postural drainage
Patient positioning to assist drainage—depends on affected lung area(s).

See also:
Endotracheal intubation, p36; Chest physiotherapy, p48; Atelectasis and pulmonary collapse, p284; Haemoptysis, p304; Inhalation injury, p306

Complications

- Hypoxaemia—from suction, loss of PEEP, etc.
- Haemodynamic disturbance affecting cardiac output, heart rate and blood pressure which may be related to high V_T, airway pressure, hypoxaemia, agitation, tracheal stimulation, etc.
- Direct trauma from suctioning.
- Barotrauma/volutrauma including pneumothorax.

General

- Adequate humidification avoids tenacious sputum and mucus plugs.
- Pain relief is important to encourage good chest excursion and cough.
- Mobilisation and encouraging deep breathing may avoid infection.

When to request urgent physiotherapy

- Collapsed lung/lobe with no air bronchogram visible, i.e. suggesting proximal obstruction rather than consolidation.
- Mucus plugging causing subsegmental collapse e.g. asthma.

When not to request urgent physiotherapy

- Clinical signs of chest infection with no secretions being produced.
- Radiological consolidation with air bronchogram but no secretions present.

See also:
Ventilatory support—indications, p4; Endotracheal intubation, p36; Tracheotomy, p38; Minitracheotomy, p40; Fibreoptic bronchoscopy, p46; Atelectasis and pulmonary collapse, p284; Acute chestinfection (1), p288; Acute chest infection (2), p290

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Cardiovascular Therapy Techniques

Defibrillation
Electrical conversion of a tachyarrhythmia to restore normal sinus rhythm. This may be an emergency procedure (when the circulation is absent or severely compromised), semi-elective (when the circulation is compromised to a

lesser degree), or elective (when synchronised cardioversion is performed to restore sinus rhythm for a non-compromising supraventricular tachycardia). Synchronisation requires initial connection of ECG leads from the patient to the defibrillator so that the shock is delivered on the R wave to minimise the risk of ventricular fibrillation. Newer, biphasic defibrillators require approximately half the energy setting of monophasic defibrillators.

Indications

- Compromised circulation, e.g. VF, VT
- Restoration of sinus rhythm and more effective cardiac output
- Lessens risk of cardiac thrombus formation

Contraindications/cautions

- Aware patient
- Severe coagulopathy
- Caution with recent thrombolysis
- Digoxin levels in toxic range

Complications

- Surface burn
- Pericardial tamponade
- Electrocution of bystanders

Technique

(see algorithm opposite).

- The chances of maintaining sinus rhythm are increased in elective cardioversion if K^+ >4.5mmol/l and plasma Mg^{2+} levels are normal.
- Prior to defibrillation, ensure self and onlookers are not in contact with patient or bed frame.
- To reduce the risk of superficial burns, replace gel/gelled pads after every 3 shocks.
- Consider resiting paddle position (e.g. anteroposterior) if defibrillation fails.
- The risk of intractable VF following defibrillation in a patient receiving digoxin is small unless the plasma digoxin levels are in the toxic range or the patient is hypovolaemic.
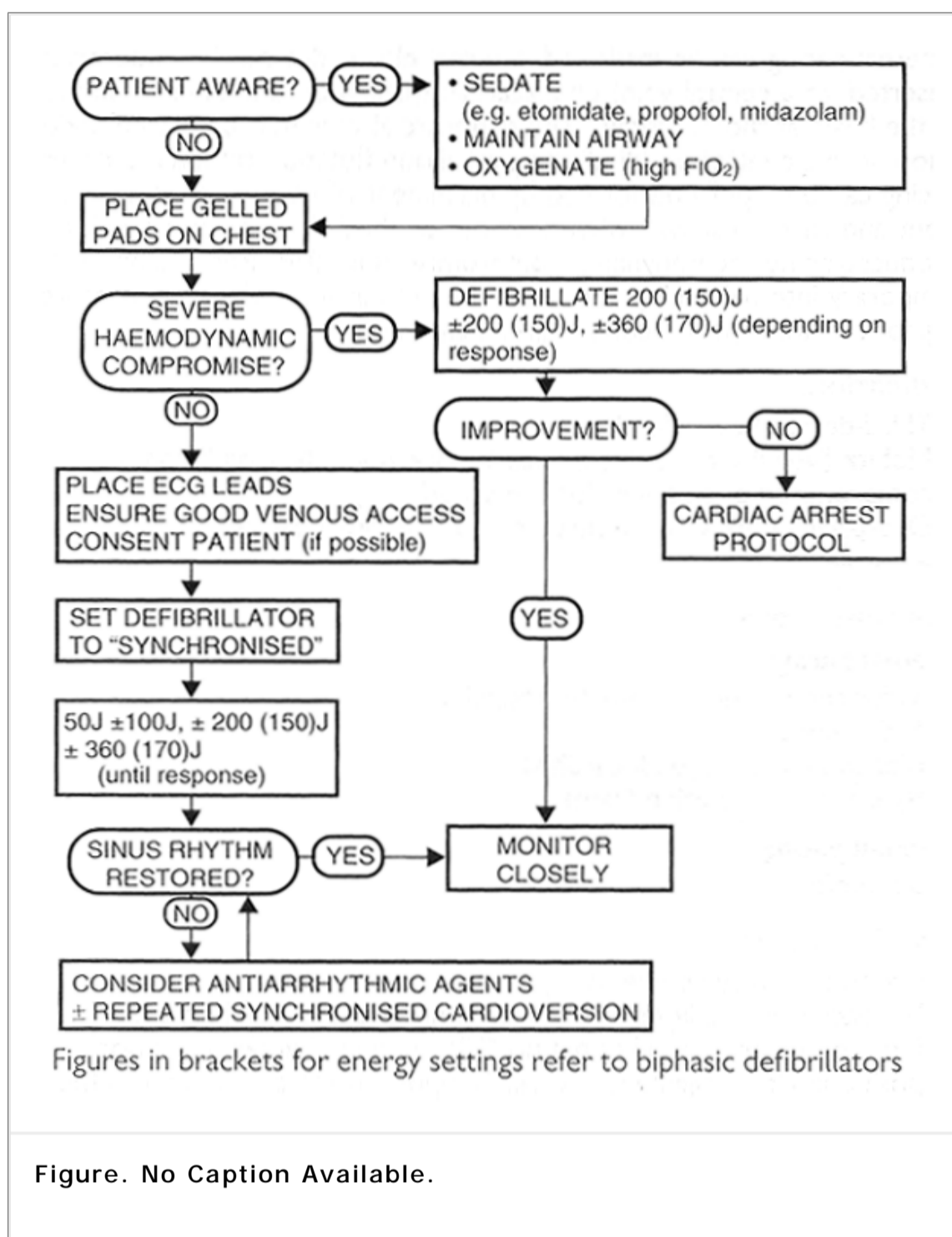
PATIENT AWARE? —(YES)→ • SEDATE
(e.g. etomidate, propofol, midazolam)
• MAINTAIN AIRWAY
• OXYGENATE (high FiO₂)

(NO)
↓

PLACE GELLED
PADS ON CHEST

SEVERE HAEMODYNAMIC COMPROMISE? —(YES)→ DEFIBRILLATE 200 (150)J
±200 (150)J, ±360 (170)J (depending on response)

(NO)

IMPROVEMENT? —(NO)→ CARDIAC ARREST PROTOCOL

PLACE ECG LEADS
ENSURE GOOD VENOUS ACCESS
CONSENT PATIENT (if possible)

(YES)

SET DEFIBRILLATOR
TO "SYNCHRONISED"

50J ±100J, ± 200 (150)J
± 360 (170)J
(until response)

SINUS RHYTHM RESTORED? —(YES)→ MONITOR CLOSELY

(NO)

CONSIDER ANTIARRHYTHMIC AGENTS
± REPEATED SYNCHRONISED CARDIOVERSION

Figures in brackets for energy settings refer to biphasic defibrillators

Figure. No Caption Available.

See also:

Chronotropes, p206; Sedatives, p238; Cardiac arrest, p272; Tachyarrhythmias, p316; Hypokalaemia, p422

Temporary pacing (1)

When the heart's intrinsic pacemaking ability fails, temporary internal or external pacing can be instituted. Internal electrodes can be endocardial (inserted via a central vein) or epicardial (placed on the external surfaceof the heart at thoracotomy). The endocardial wire may be placed under fluoroscopic control or 'blind' using a balloon flotation catheter. External pacing can be rapidly performed by placement of two electrodes on the front and rear chest wall when asystole or third degree heart block has produced acute haemodynamic compromise. It is often used as a bridge to temporary internal pacing. It can also be used as a prophylactic measure, e.g. for Mobitz Type II second-degree heart block.

Indications

- Third-degree heart block
- Mobitz Type II second-degree heart block when the circulation iscompromised or an operation is planned
- Overpacing (rarely; more successful with internal pacing)
- Asystole

Complications

Internal pacing

- As for central venous catheter insertion
- Arrhythmias
- Infection (including endocarditis)
- Myocardial perforation (rare)

External pacing

- Discomfort

Troubleshooting

Failure to pace may be due to:

1. No pacemaker spikes seen—check connections, check battery.

2. No capture (pacing spikes but no QRS complex following)—poor positioning/dislodgement of wire. Temporarily increase output as this may regain capture. Reposition/replace internal pacing wire.

General

1. Check threshold daily as it will rise slowly over 48–96h, probably due to fibrosis occurring around the electrodes.

2. Overpacing is occasionally indicated for a tachycardia not responding to antiarrhythmic therapy or cardioversion. For SVT, pacing is usually attempted with the wire sited in the right atrium. Pace at rate 20–30bpm above patient's heart rate for 10–15s, then either decrease rate immediately to 80bpm or slowly, by 20bpm every 5–10s.

3. If overpacing fails, underpacing may be attempted with the wire situated in either atrium (for SVT) or, usually, ventricle (for either SVT or VT). A paced rate of 80–100bpm may produce a refractory period sufficient to suppress the intrinsic tachycardia.

4. Epicardial pacing performed during cardiac surgery requires siting of either two epicardial electrodes or one epicardial and one skin electrode (usually a hypodermic needle). The pacing threshold of epicardial wires rises quickly and may become ineffective after 1–2 days.

5. In asystole, an electrical rhythm produced by pacing does not guarantee an adequate cardiac output is being generated.

See also:

Temporary pacing (2)

Technique (for endocardial electrode placement)

1. If using fluoroscopy, move patient to X-ray suite or place lead shields around bed area. Place patient on 'screening table'. Staff should wear lead aprons.

2. Use aseptic technique throughout. Insert 6Fr sheath in internal jugular or subclavian vein. Suture in position.

3. Connect pacing wire electrodes to pacing box (black = negative polarity = distal, red = positive polarity = proximal). Set pacemakerto demand. Check box is working and battery charge adequate. Turn pacing rate to ≥30bpm above patient's intrinsic rhythm. Set voltage to 4V.

4. Insert pacing wire through sheath into central vein. If using balloon catheter, insert to 15–20cm depth then inflate balloon. Advance catheter, viewing ECG monitor for change in ECG morphology and capture of pacing rate. If using screening, direct wire toward the apex of the right ventricle. Approximate insertion depth from a neck veinis 35–40cm.

5. If pacing impulses not captured, (deflate balloon), withdraw wire to 15cm insertion depth then repeat step 4.

6. Once pacing captured, decrease voltage by decrements to determine threshold at which pacing is no longer captured. Ideal position determined by a threshold ≤0.6V. If not achieved, re-position wire.

7. If possible, ask patient to cough to check that wire does not dislodge.

8. Set voltage at 3 × threshold and set desired heart rate on 'demand' mode. Tape wire securely to patient to prevent dislodgement.

Technique (for external pacing)

1. Connect pacing wire gelled electrodes to pacemaker. Place black (= negative polarity) electrode on the anterior chest wall to the left of the lower sternum and red (= positive polarity) electrode to the corresponding position on the posterior hemithorax.

2. Connect ECG electrodes from ECG monitor to external pacemaker and another set of electrodes from pacemaker to patient

3. Set pacemaker to demand. Turn pacing rate to ≥30bpm above patient's intrinsic rhythm. Set current to 70mA.

4. Start pacing. Increase current (by 5mA increments) until pacing rate captured on monitor.

5. If pacing rate not captured at current of 120–130mA resite electrodes and repeat steps 3–4.

6. Once pacing captured, set current at 5–10mA above threshold.

See also:

Intra-aortic balloon counterpulsation

Principle

A 30–40ml balloon is placed in the descending aorta. The balloon is inflated with helium during diastole, thus increasing diastolic blood pressure above the balloon. This serves to increase coronary and cerebral perfusion. The balloon is deflated during systole, thus decreasing peripheral resistance and increasing stroke volume. No pharmacological technique exists which can increase coronary blood flow while reducing peripheral resistance. Intra-aortic balloon counterpulsation may improve cardiac performance in situations where drugs are ineffective.

Indications

The most obvious indication is to support the circulation where a structural cardiac defect is to be repaired surgically. However, it may be used in acute circulatory failure in any situation where resolution of the cause of the cardiac dysfunction is expected. In acute myocardial infarction, resolution of peri-infarct oedema may allow spontaneous improvement in myocardial function; the use of intra-aortic balloon counterpulsation may provide temporary circulatory support and promote myocardial healing by improving myocardial blood flow. Other indications include acute myocarditis and poisoning with myocardial depressants. Intra-aortic balloon counterpulsation should not be used in aortic regurgitation since the increase in diastolic blood pressure would increase regurgitant flow.

Insertion of the balloon

The usual route is via a femoral artery. Percutaneous Seldinger catheterisation (with or without an introducer sheath) provides a rapid and safe technique with minimal arterial trauma and bleeding. Open surgical catheterisation may be necessary in elderly patients with atheromatous disease. The balloon position should be checked on a CXR to ensure that the radio-opaque tip is at the level of the 2nd intercostal space. Ensure the left radial pulse is not lost.

Anticoagulation

The presence of a large foreign body in the aorta requires systemic anticoagulation to prevent thrombosis. The balloon should not be left deflated for longer than a minute while *in situ* otherwise thrombosis may occur despite anticoagulation.

Control of balloon inflation and deflation

Helium is used to inflate the balloon, its low density facilitating rapid transfer from pump to balloon. Inflation is commonly timed to the 'R' wave of the ECG, although timing may be taken from an arterial pressure waveform. Minor adjustment may be made to the timing to ensure that inflation occurs immediately after closure of the aortic valve (after the dicrotic notch of the arterial pressure waveform) and deflation occurs at the end of diastole. The filling volume of the balloon can be varied up to the maximum balloon volume. The greater the filling volume, the greater the circulatory augmentation. The rate at which balloon inflation occurs may coincide with every cardiac beat or every 2nd or 3rd cardiac beat. Slower rates are necessary in tachyarrhythmias. Weaning of intra-aortic balloon counterpulsation may be achieved by reducing augmentation or the rate of inflation.

See also:

Renal Therapy Techniques

Haemo(dia)filtration (1)

These are alternatives to dialysis that require a pressurised, purified water supply, more expensive equipment and operator expertise, and a greater risk of haemodynamic instability due to rapid fluid and osmotic shifts. Haemo(dia)filtration can be arteriovenous, using the patient's blood pressure to drive blood through the haemofilter, or pumped veno-venous. The latter is advantageous in that it is not dependent on the patient's blood pressure and the pump system incorporates alarms and safety features. Veno-venous haemo(dia)filtration is increasingly the technique of choice. Blood is usually drawn and returned via a 10–12Fr double lumen central venous catheter.

Indications

- Azotaemia (uraemia)

- Hyperkalaemia

- Anuria/oliguria; to make space for nutrition

- Severe metabolic acidosis of non-tissue hypoperfusion origin

- Fluid overload

- Drug removal

- Hypothermia/hyperthermia

Techniques

Numerous including haemofiltration, haemodiafiltration, ultrafiltration, continuous ultrafiltration with intermittent dialysis (CUPID). Filtrate is usually removed at 1–2l/h and fluid balance adjusted by varying the fluid replacement rate. High volume haemofiltration involves much higher clearances (e.g. 35l in a 4h period) though variable outcomes are reported in randomised studies.

Creatinine and potassium clearances are higher with diafiltration though filtration alone is usually sufficient provided an adequate ultrafiltrate volume is achieved (1000ml/h = creatinine clearance of 16ml/min).

Membranes

Usually polyacrylonitrile, polyamide or polysulphone. May be hollow fibre or flat-plate in design. Surface area usually 0.6–1m^2.

Replacement fluid

A buffered balanced electrolyte solution is given to buffer acidaemia and achieve the desired fluid balance. Buffers include lactate (metabolised by liver to bicarbonate), acetate (metabolised by muscle), and bicarbonate. Acetate causes the most haemodynamic instability and is rarely used in the critically ill. Bicarbonate solutions may be more efficient than lactate at reversing severe metabolic acidosis, but outcome benefit has yet to be demonstrated from its use and care is needed with co-administered calcium since calcium bicarbonate may crystallise. In liver failure a lactate buffer may not be adequately metabolised. Similarly, in poor perfusion states, the muscle may not be able to metabolise an acetate buffer.

An increasing metabolic alkalosis may be due to excessive buffer. In this case, use a 'low lactate' (i.e. 30mmol/l) replacement fluid. Potassium can be added, if necessary, to maintain normokalaemia. Having 20mmol KCl in a 4.5l bag provides a concentration of 4.44mmol/l. K$^+$ clearance is increased by decreasing the concentration within the replacement fluid or the dialysate.
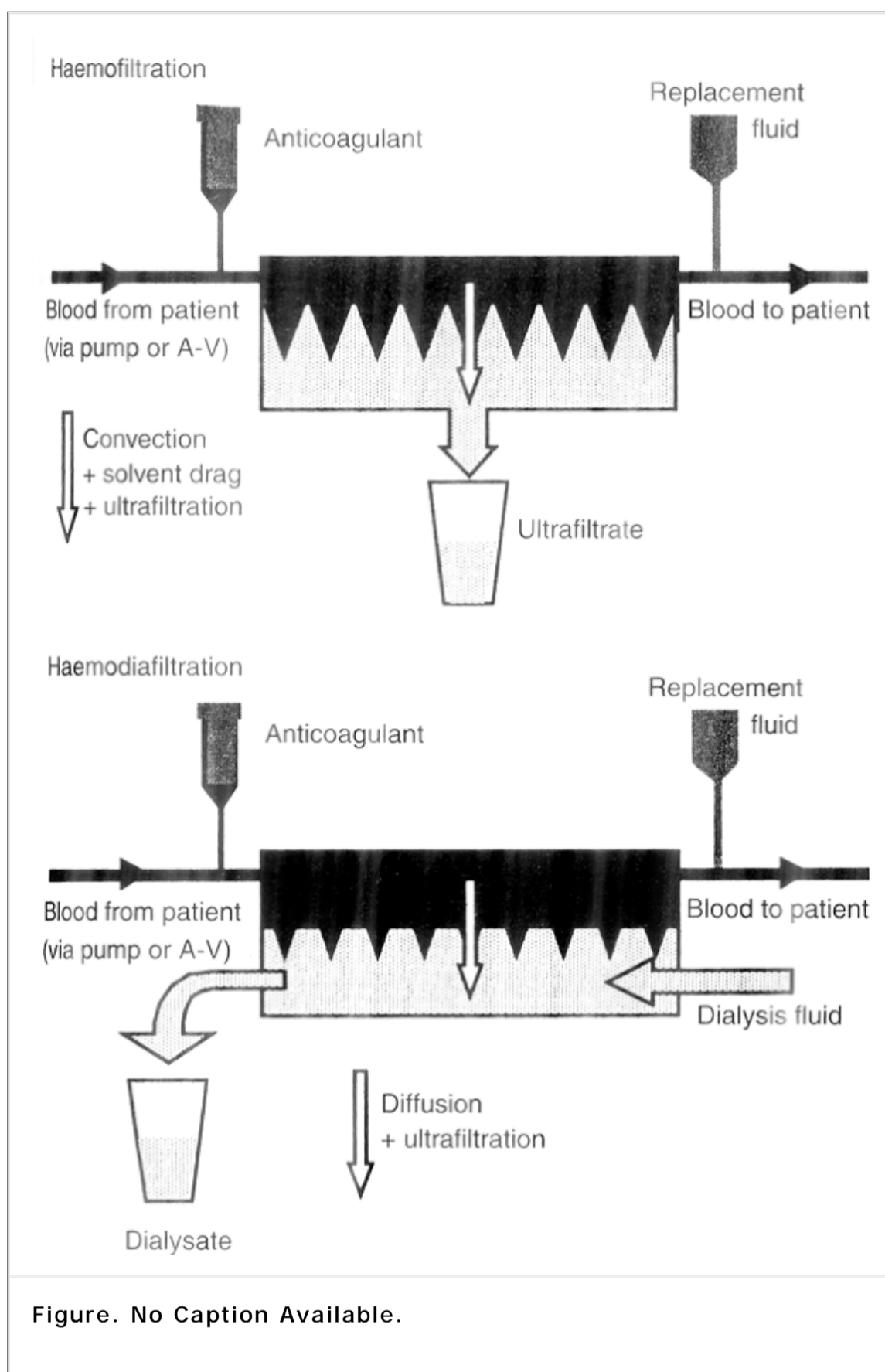
Figure. No Caption Available.

Key trials

Ronco C, et al. Effects of different doses in continuous veno-venous haemofiltration on outcomes of acute renal failure: a prospective randomised trial. Lancet 2000; 356:26–30

Bouman CS, et al. Effects of early high-volume continuous venovenous hemofiltration on survival and recovery of renal function in intensive care patients with acute renal failure: a prospective, randomized trial.

Crit Care Med 2002; 30:2205–11

See also:

Haemo(dia)filtration (2)

Anticoagulation

- Anticoagulation of the circuit is usually with unfractionated heparin (200–2000IU/h), or a prostanoid (prostacyclin or PGE_1) at 2–10ng/kg/min, or a combination of the two. Little experience is available on the use of low molecular weight heparin, citrate and other anticoagulants such as hirudin.

- No anticoagulant may be needed if the patient is auto-anticoagulated.

- Premature clotting may be due to mechanical kinking/obstruction of the circuit, insufficient anticoagulation,

inadequate blood flow rates or to lack of endogenous anticoagulants (antithrombin III, heparin cofactor II).

- Usual filter lifespan should be at least 2 days but is often decreased in septic patients due to decreased endogenous anticoagulant levels. In this situation, consider use of fresh frozen plasma, a synthetic protease inhibitor such as aprotinin, or antithrombin III replacement (costly).

Filter blood flow

Flow through the filter is usually 100–200ml/min. Too slow a flow rate promotes clotting. Too high a flow rate will increase transmembrane pressures and decrease filter lifespan without significant improvement in clearance of 'middle molecules' (e.g. urea).

Complications

- Disconnection leading to haemorrhage.
- Infection risk (sterile technique must be employed).
- Electrolyte, acid–base or fluid imbalance (excess input or removal).
- Haemorrhage (vascular access sites, peptic ulcers) related to anticoagulation therapy or consumption coagulopathy. Heparin-induced thrombocytopenia may rarely occur.

Cautions

- Haemodynamic instability related to hypovolaemia (especially at start).
- Vasoactive drug removal by the filter (e.g. catecholamines).
- Membrane biocompatibility problems (especially with cuprophane).
- Drug dosages may need to be revised (consult pharmacist).
- Amino acid losses through the filter.
- Heat loss leading to hypothermia.
- Masking of pyrexia

Peritoneal dialysis

A slow form of dialysis, utilising the peritoneum as the dialysis membrane. Slow correction of fluid and electrolyte disturbance may be better tolerated by critically ill patients and the technique does not require complex equipment. However, treatment is labour intensive and there is considerable risk of peritoneal infection. It has been largely superseded by haemofiltration in most intensive care units.

Peritoneal access

For acute peritoneal dialysis a trochar and cannula are inserted through a small skin incision under local anaesthetic. The skin is prepared and draped as for any sterile procedure. The commonest approach is through a small midline incision 1cm below the umbilicus. The subcutaneous tissues and peritoneum are punctured by the trocar which is withdrawn slightly before the cannula is advanced towards the pouch of Douglas. In order to avoid damage to intra-abdominal structures 1–2l warmed peritoneal dialysate may be infused into the peritoneum by a standard, short intravascular cannula prior to placement of the trocar and cannula system. If the midline access site is not available an alternative is to use a lateral approach, lateral to a line joining the umbilicus and the anterior superior iliac spine (avoiding the inferior epigastric vessels).

Dialysis technique

Warmed peritoneal dialysate is infused into the peritoneum in a volume of 1–2l at a time. During the acute phase, fluid is flushed in and drained continuously (i.e. with no dwell time). Once biochemical control is achieved it is usual to leave fluid in the peritoneal cavity for 4-6h before draining. Heparin (500IU/l) may be added to the first 6 cycles to prevent fibrin catheter blockage. Thereafter, it is only necessary if there is blood or cloudiness in the drainage fluid.

Peritoneal dialysate

The dialysate is a sterile balanced electrolyte solution with glucose at 75mmol/l for a standard fluid or 311mmol/l for a hypertonic fluid (used for greater fluid removal). The fluid is usually potassium free since potassium exchanges slowly in peritoneal dialysis, although potassium may be added if necessary.

Complications

- Fluid leak

    Poor drainage

> Steroid therapy

> Obese or elderly patient

- Catheter blockage

> Bleeding

> Omental encasement

- Infection

> White cells >50/ml, cloudy drainage fluid

- Hyperglycaemia

> Absorption of hyperosmotic glucose

- Diaphragm splinting

Treatment of infection

It is possible to sterilise the peritoneum and catheter by adding appropriate antibiotics to the dialysate. Suitable regimens include:

- Cefuroxime 500mg/l for 2 cycles then 200mg/l for 10 days

- Gentamicin 8mg/l for 1 cycle daily

See also:

Plasma exchange

Indications

Plasma exchange may be used to remove circulating toxins or to replace missing plasma factors. It may be used in sepsis (e.g. meningococcaemia). In patients with immune mediated disease, plasma exchange is usually a temporary measure while systemic immunosuppression takes effect. There are some immune mediated diseases (e.g. Guillain–Barré syndrome, thrombotic thrombocytopenic purpura) where an isolated rather than a continuous antibody–antigen reaction can be treated with early plasma exchange and no follow-up immunosuppression. Most diseases require a daily 3–4l plasma exchange repeated for at least 4 further occasions over 5–10 days.

Techniques

Cell separation by centrifugation

Blood is separated into components in a centrifuge. Plasma (or other specific blood components) are discarded and a plasma replacement fluid is infused in equal volume. Centrifugation may be continuous where blood is withdrawn and returned by separate needles, or intermittent where blood is withdrawn, separated and then returned via the same needle.

Membrane filtration

Plasma is continuously filtered through a large pore filter (molecular weight cut-off typically 1,000,000Da). The plasma is discarded and replaced by infusion of an equal volume of replacement fluid. The technique is similar to haemofiltration and uses the same equipment.

Replacement fluid

Most patients will tolerate replacement with a plasma substitute. Our preference is to replace plasma loss with equal volumes of 6% hydroxy-ethyl starch and 5% albumin. However, some use partial crystalloid replacement and others use all albumin replacement. Some fresh frozen plasma will be necessary after the exchange to replace coagulation factors. The only indication to replace plasma loss with all fresh frozen plasma is where plasma exchange is being performed to replace missing plasma factors.

Complications

- Circulatory instability

> Intravascular volume changes

> Removal of circulating catecholamines

> Hypocalcaemia

- Reduced intravascular COP

> If replacement with crystalloid

- Infection

    Reduced plasma opsonisation

- Bleeding

    Removal of coagulation factors

Indications

Autoimmune disease
Goodpasture's syndrome

Guillain–Barré syndrome

Myasthenia gravis

Pemphigus

Rapidly progressive glomerulonephritis

SLE

Thrombotic thrombocytopenic purpura

Immunoproliferative disease
Cryoglobulinaemia

Multiple myeloma

Waldenstrom's macroglobulinaemia

Poisoning
Paraquat

Others
Meningococcal septicaemia (possible benefit)

Sepsis (possible benefit)

Reye's syndrome

See also:

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Gastrointestinal Therapy Techniques

Sengstaken-type tube
Used to manage oesophageal variceal haemorrhage that continues despite pharmacological ± per-endoscopic therapy. The device (Sengstaken– Blakemore or similar) is a large-bore rubber tube usually containing two balloons (oesophageal and gastric) and two further lumens (oesophageal and gastric) that open above and below the balloons. This device works usually by the gastric balloon alone compressing the varices at the cardia. Inflation of the oesophageal balloon is rarely necessary.

Insertion technique
The tubes are usually kept in the fridge to provide added stiffness for easier insertion.

1. The patient often requires judicious sedation or mechanical ventilation (as warranted by conscious state/level of agitation) prior to insertion.

2. Check balloons inflate properly beforehand. Lubricate end of tube.

3. Insert via mouth. Place to depth of 55–60cm, i.e. to ensure gastric balloon is in stomach prior to inflation.

4. Inflate gastric balloon with water to volume instructed by manufacturer (usually ♠200ml). A small amount of

radio-opaque contrast may be added. Negligible resistance to inflation should be felt. Clamp gastric balloon lumen.

5. Pull tube back until resistance is felt, i.e. gastric balloon is at cardia. Fix tube in place by applying counter-traction at the mouth. Old-fashioned methods, such as attaching the tube to a free-hanging litre bag of saline, have been superseded by more manageable techniques. For example, two wooden tongue depressors, 'thickened' by having Elastoplast wound around them, are placed either side of the tube at the mouth and then attached to each other at both ends by more Elastoplast. The tube remains gripped at the mouth/cheek by the attached tongue depressors but can be retracted until adequate but not excessive traction is being applied.

6. Perform X-ray to check satisfactory position of gastric balloon.

7. If bleeding continues (continued large aspirates from gastric or oesophageal lumens), inflate oesophageal balloon (approx 50ml).

Subsequent management

1. The gastric balloon is usually kept inflated for 12–24h and deflated prior to endoscopy ± sclerotherapy. The traction on the tube should be tested hourly by the nursing staff. The oesophageal lumen should be placed on continuous drainage while enteral nutrition and administration of drugs can be given via the gastric lumen.

2. If the oesophageal balloon is used, deflate for 5–10min every 1–2h to reduce the risk of oesophageal pressure necrosis. Do not leave oesophageal balloon inflated for longer than 12h after sclerotherapy.

3. The tube may need to stay *in situ* for 2–3 days though periods of deflation should then be allowed.

Complications

- Aspiration
- Perforation
- Ulceration
- Oesophageal necrosis

See also:

Upper gastrointestinal endoscopy
Oesophago-gastro-duodenoscopy is identical in ventilated and non-ventilated patients, though a protected airway ± sedated status usually facilitates the procedure.

Indications

- Investigation of upper gastrointestinal signs/symptoms. e.g. bleeding, pain, mass, obstruction
- Therapeutic, e.g. sclerotherapy for varices, local epinephrine (adrenaline) injection for discrete bleeding points, e.g. in ulcer base
- Placement of nasojejunal tube (when gastric atony prevents enteral feeding) or percutaneous gastrostomy (PEG)
- ERCP—unusual in the ICU patient

Complications

- Local trauma causing haemorrhage or perforation
- Abdominal distension compromising respiratory function

Contraindications/cautions

- Severe coagulopathy should ideally be corrected

Procedure
Upper gastrointestinal endoscopy should be performed by an experienced operator to minimise the duration and trauma of the procedure, and to minimise gaseous distension of the gut.

1. The patient is usually placed in a lateral position though can be supine if intubated.

2. Increase FIO$_2$ and ventilator pressure alarm settings. Consider increasing sedation and adjusting ventilator mode.

3. Monitor ECG, SPO$_2$, airway pressures and haemodynamic variables throughout. If patient is on pressure support or pressure control ventilatory modes also monitor tidal volumes. The operator should cease the procedure, at least temporarily, if the patient becomes compromised.

4. At the end of the procedure the operator should aspirate as much air as possible out of the gastrointestinal tract to decompress the abdomen.

See also:

Nutrition

Nutrition—use and indications

Malnutrition leads to poor wound healing, post-operative complications and sepsis. Adequate nutritional support is important for critically ill patients and should be provided early during the illness. Evidence for improved outcome from early nutritional support exists for patients with trauma and burns. Enteral nutrition is indicated when swallowing is inadequate or impossible but gastrointestinal function is otherwise intact. Parenteral nutrition is indicated where the gastrointestinal tract cannot be used to provide adequate nutritional support, e.g. obstruction, ileus, high small bowel fistula or malabsorption. Parenteral nutrition may be used to supplement enteral nutrition where gastrointestinal function allows partial nutritional support.

Consequences of malnutrition

Underfeeding	Overfeeding
Loss of muscle mass	Increased VO$_2$
Reduced respiratory function	Increased VCO$_2$
Reduced immune function	Hyperglycaemia
Poor wound healing	Fatty infiltration of liver
Gut mucosal atrophy	
Reduced protein synthesis	

Calorie requirements

Various formulae exist to calculate the patient's basal metabolic rate but are misleading in critical illness. Metabolic rate can be measured by indirect calorimetry but most patients are assumed to require 2000–2700Cal/ day, or less if starved or underweight.

Nitrogen requirements

Nitrogen excretion can be calculated in the absence of renal failure according to the 24h urea excretion:

Nitrogen (g/24h) = 2 + Urinary urea (mmol/24h) × 0.028

However, as with most formulae, this method lacks accuracy. Most patients require 7–14g/day.

Other requirements

The normal requirements of substrates, vitamins and trace elements are tabled opposite. Most long-term critically ill patients require folic acid and vitamin supplementation during nutritional support, e.g. Solvito. Trace elements are usually supplemented in parenteral formulae but should not be required during enteral nutrition.

Normal daily requirements (for a 70kg adult)	
Water	2100ml
Energy	2000–2700Cal
Nitrogen	7–14g
Glucose	210g
Lipid	140g
Sodium	70–140mmol
Potassium	50–120mmol
Calcium	5–10mmol
Magnesium	5–10mmol
Phosphate	10–20mmol
Vitamins	
Thiamine	16–19mg
Riboflavin	3–8mg
Niacin	33–34mg
Pyridoxine	5–10mg
Folate	0.3–0.5mg
Vitamin C	250–450mg
Vitamin A	2800–3300iu
Vitamin D	280–330iu
Vitamin E	1.4–1.7iu
Vitamin K	0.7mg
Trace elements	
Iron	1–2mg
Copper	0.5–1.0mg
Manganese	1–2µg
Zinc	2–4mg
Iodide	70–140µg
Fluoride	1–2mg

Enteral nutrition

Routes include naso-gastric, naso-duodenal/jejunal, gastrostomy and jejunostomy. Nasal tube feeding should be via a soft, fine-bore tube to aid patient comfort and avoid ulceration of the nose or oesophagus. Prolonged enteral feeding may be accomplished via a percutaneous/peroperative gastrostomy or peroperative jejunostomy. Enteral feeding provides a more complete diet than parenteral nutrition, maintains structural integrity of the gut, improves bowel adaptation after resection and reduces infection risk.

Feed composition

Most patients tolerate iso-osmolar, non-lactose feed. Carbohydrates are provided as sucrose or glucose polymers; protein as whole protein or oligopeptides (may be better absorbed than free amino acids in 'elemental' feeds); fats as medium chain or long chain triglycerides. Medium chain triglycerides are better absorbed. Standard feed is formulated at 1Cal/ml. Special feeds are available, e.g. high fibre, high protein-calorie, restricted salt, high fat or concentrated (1.5 or 2Cal/ml) for fluid restriction. Immune-enhanced feeds (e.g. glutamine-enriched or Impact ®, a formula supplemented with nucleotides, arginine and fish oil) may reduce nosocomial infections but no evidence of outcome benefit has been shown from large prospective studies.

Management of enteral nutrition

Once a decision is made to start enteral nutrition, 30ml/h full strength standard feed may be started immediately. Starter regimens incorporating dilute feed are not necessary. After 4h at 30ml/h the feed should be stopped for 30min prior to aspiration of the stomach. Since gastric juice production is increased by the presence of a nasogastric tube, it is reasonable to accept an aspirate of <200ml as evidence of gastric emptying and therefore to increase the infusion rate to 60ml/h. This process is repeated until the target feed rate is achieved. Thereafter, aspiration of the stomach can be reduced to 8hrly. If the gastric aspirate volume is >200ml the infusion rate is not increased but the feed is continued. If aspirates remain at high volume despite measures to promote gastric emptying (e.g. metoclopramide or erythromycin) then either bowel rest, nasoduodenal/nasojejunal feeding or parenteral nutrition should be considered.

Complications

- Tube placement: tracheobronchial intubation, nasopharyngeal perforation, intracranial penetration (basal skull fracture), oesophageal perforation
- Reflux
- Pulmonary aspiration
- Nausea and vomiting
- Abdominal distension is occasionally reported with features including a tender, distended abdomen and an increasing metabolic acidosis. Laparotomy and bowel resection may be necessary in severe cases
- Diarrhoea: large volume, bolus feeding, high osmolality, infection, lactose intolerance, antibiotic therapy, high fat content
- Constipation
- Metabolic: dehydration, hyperglycaemia, electrolyte imbalance

Key trial

Atkinson S, et al. A prospective, randomized, double-blind, controlled clinical trial of enteral immunonutrition in the critically ill. Crit Care Med 1998; 26:1164–72

See also:

Parenteral nutrition

Feed composition

Carbohydrate is normally provided as concentrated glucose. 30–40% of total calories are usually given as lipid (e.g. soya bean emulsion). The nitrogen source is synthetic, crystalline L-amino acids which should contain appropriate quantities of all essential and most non-essential amino acids. Carbohydrate, lipid and nitrogen sources are usually mixed into a large bag in a sterile pharmacy unit. Vitamins, trace elements and appropriate electrolyte concentrations can be achieved in a single infusion, thus avoiding multiple connections. Volume, protein and calorie content of the feed should be determined on a daily basis in conjunction with the dietitian.

Choice of parenteral feeding route

Central venous

A dedicated catheter (or lumen of a multi-lumen catheter) is placed under sterile conditions. For long-term feeding a subcutaneous tunnel is often used to separate skin and vein entry sites. This probably reduces the risk of infection and clearly identifies the special purpose of the catheter. Ideally, blood samples should not be taken nor other injections or infusions given via the feeding lumen. The central venous route allows infusion of hyperosmolar solutions, providing adequate energy intake in reduced volume.

Peripheral venous

Parenteral nutrition via the peripheral route requires a solution with osmolality <800mOsmol/kg. Either the volume must be increased or the energy content (particularly from carbohydrate) reduced. Peripheral cannulae sites must be changed frequently.

Complications

- Catheter related   Misplacement
                           Infection
                           Thromboembolism
- Fluid excess
- Hyperosmolar hyperglycaemic state
- Electrolyte imbalance
- Hypophosphataemia
- Metabolic acidosis   Hyperchloraemia
                           Metabolism of cationic amino acids
- Rebound hypoglycaemia
           High endogenous insulin levels
- Vitamin deficiency   Folate   Pancytopenia
                           Thiamine   Encephalopathy
                           Vitamin K   Hypoprothrombinaemia
- Vitamin excess   Vitamin A   Dermatitis
                       Vitamin D   Hypercalcaemia
- Fatty liver

See also:

Special Support Surfaces

Special support surfaces

Pressure sores

Pressure sores occur due to compression of tissue between bone and the support surface and due to shearing forces, friction and maceration of tissues against the support surface. The use of special beds attempts to reduce the pressure at the contacting skin surface to a level lower than the capillary occlusion pressure. In the majority of cases it is sufficient to minimise the time that the support surface contacts any one area of skin by position changes.

Factors suggesting the need for a special bed

- Patients with severely restricted mobility due to traction or cardiorespiratory instability cannot be turned frequently, if at all.

- Patients with decreased skin integrity, e.g. burns, pressure sores already present, chronic steroid use, diabetes mellitus.

- Patients on vasoactive drug infusions.

Types of special support surface

Air mattress
This either replaces or is placed on top of a standard hospital bed mattress. They provide minimum reduction in contact pressure but should be considered as minimum support for any patient with the above factors.

Low air loss bed
These purpose-built pressure-relieving beds allow easier patient mobility than other support surfaces. Contact pressure may still be higher than capillary occlusion pressure so positioning is still required. Patients who are haemodynamically unstable should usually be managed on a low air loss bed, particularly if receiving vasoconstrictor drugs. The presence of pressure sores with intact skin is an indication for a low air loss bed. Rotational low air loss beds allow automated lateral rotation at variable time intervals to facilitate chest drainage. These may also be useful where manual positioning is impractical.

Air fluidised bed
This is the only support surface that consistently lowers contact pressure to below capillary occlusion pressure. Consequently, patients with severe cardiorespiratory instability, who cannot be turned, and patients with pressure sores with broken skin benefit most. The additional ability to control the temperature of the immediate environment is an advantage in hypothermic patients and those with large surface area burns. Any exudate from the skin is adsorbed into the silicone beads on which the patient floats. This drying effect is particularly useful in major burns (although it must be taken into account for fluid replacement therapy). The air fluidised bed also has a role in pain relief.

Respiratory Monitoring

Pulse oximetry
Continuous non-invasive monitoring of arterial oxygen saturation by placement of a probe emitting red and near-infrared light over the pulse on digit, earlobe, cheek or bridge of nose. It is unaffected by skin pigmentation, hyperbilirubinaemia or anaemia (unless profound).

Physics
The colour of blood varies with oxygen saturation due to the optical properties of the haem moiety. As the Hb molecule gives up O_2 it becomes less permeable to red light and takes on a blue tint. Saturation is determined spectrophotometrically by measuring the 'blueness', utilising the ability of compounds to absorb light at a specific wavelength. The use of two wavelengths (650 and 940nm) permits the relative quantities of reduced and oxyhaemoglobin to be calculated, thereby determining saturation. The arterial pulse is used to provide time points to allow subtraction of the constant absorption of light by tissue and venous blood. The accuracy of pulse oximetry is within 2% above 70% SaO_2.

Indications

- Continuous monitoring of arterial oxygen saturation.

Cautions

- As only two wavelengths are used, pulse oximetry measures functional rather than fractional oxyhaemoglobin saturation. Erroneously high readings are given with carboxyhaemoglobin and methaemoglobin.

- With poor peripheral perfusion or intense vasoconstriction the reading may be inaccurate ('fail soft') or, in newer models, absent ('fail hard').

- Motion artefacts and high levels of ambient lighting may affect readings.

- Erroneous signal may be produced by significant venous pulsation from tricuspid regurgitation or venous congestion. Venous pulsatility accounts for differences between ear and finger SpO_2 in the same subject.

- Ensure a good LED signal indicator or a pulse waveform (if available) is seen on the monitor.

- Vital dyes (e.g. methylthioninium chloride (methylene blue), indocyanine green) may affect SpO_2 readings.

See also:

Oxygen therapy, p2; Ventilatory support—indications, p4; IPPV—adjusting the ventilator, p10; Continuous positive airway pressure, p26; Endotracheal intubation, p36; Tracheotomy, p38; Fibreoptic bronchoscopy, p46; Chest physiotherapy, p48; Upper gastrointestinal endoscopy, p74; Blood gas analysis, p100; Basic resuscitation, p270; Dyspnoea, p278; Respiratory failure, p282; Acute chest infection (1), p288; Acute chest infection (2), p290; Acute respiratory distress syndrome (1), p292; Acute respiratory distress syndrome (2), p294; Asthma—general management, p296; Asthma—ventilatory management, p298; Pneumothorax, p300; Poisoning—general principles, p452; Post-operative intensive care, p534

CO_2 monitoring

Capnography

For capnography, respiratory gases must be sampled continuously and measured by a rapid response device. Since CO_2 has an absorption band in the infrared spectrum, measurement is facilitated in gas mixtures. Other gases can interfere with infrared absorption by CO_2. This may be overcome by calibrating the instrument with known concentrations of CO_2 in the required measurement range, diluted with a gas mixture similar to exhaled gas.

The capnogram

The CO_2 concentration of exhaled gas consists of 4 phases (see figure). The presence of significant concentrations of CO_2 in phase 1 implies rebreathing of exhaled gas. Failure of an expiratory valve to open is the most likely cause of rebreathing during manual ventilation, although an inadequate flow of fresh gas into a rebreathing bag is a common cause. The slope of phase 3 is dependent on the rate of alveolar gas exchange. A steep slope may indicate ventilation-perfusion mismatch since alveoli that are poorly ventilated but well perfused discharge late in the respiratory cycle. A steep slope is seen in patients with significant auto-PEEP.

Colorimetric devices

The underlying principle is that the change in pH produced by different CO_2 concentrations in solution will change the colour of an indicator. These are small devices that fit onto an endotracheal tube or the ventilator circuit and respond rapidly (up to 60 breaths/min). They can be affected by excessive humidity and generally only work in the range 0–4% CO_2. They are useful to confirm tracheal intubation, during patient transfer and in the cardiac arrest situation.

End-tidal PCO_2

End-tidal PCO_2 approximates $PaCO_2$ in patients with normal lung function. In ICU patients pulmonary function is rarely normal, thus end-tidal PCO_2 is a poor approximation of $PaCO_2$. Large differences may represent an increased dead space to tidal volume ratio, poor pulmonary perfusion or intrapulmonary shunting. A progressive rise in end-tidal PCO_2 may represent hypoventilation, airway obstruction or increased CO_2 production due to increased metabolic rate. End-tidal PCO_2 falls with hyperventilation and in low cardiac output states. It is absent with ventilator disconnection and during cardiac arrest but rises with effective CPR or restoration of a spontaneous circulation.

Dead space to tidal volume ratio

The arterial to end-tidal PCO_2 difference may be used to calculate the physiological dead space to tidal volume ratio via the Bohr equation:

$$\frac{V_D}{V_T} = \frac{PaCO_2}{PetCO_2}.$$

In health a value between 30 and 45% should be expected.

The components of the normal capnogram
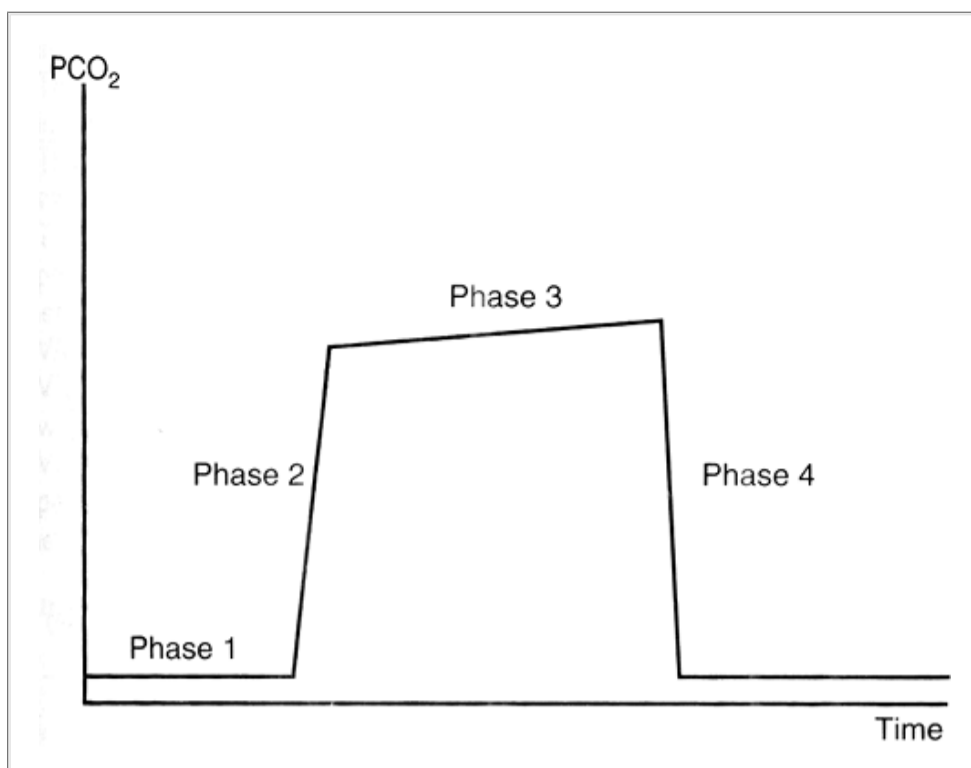
Figure. No Caption Available.

Phase 1
During the early part of the exhaled breath anatomical dead space and sampling device dead space gas are sampled. There is negligible CO_2 in phase 1.

Phase 2
As alveolar gas begins to be sampled there is a rapid rise in CO_2 concentration.

Phase 3
Phase 3 is known as the alveolar plateau and represents the CO_2 concentration in mixed expired alveolar gas. There is normally a slight increase in PCO_2 during phase 3 as alveolar gas exchange continues during expiration. Airway obstruction or a high rate of CO_2 production will increase the slope. End-tidal PCO_2 will be less than the PCO_2 of ideal alveolar gas since the sampled exhaled gas is mixed with alveolar dead space gas.

Phase 4
As inspiration begins there is a rapid fall in sample PCO_2.

See also:
Ventilatory support—indications, p4; IPPV—adjusting the ventilator, p10; Endotracheal intubation, p36; Tracheotomy, p38; Fibreoptic bronchoscopy, p46; Blood gas analysis, p100; Basic resuscitation, p270

Pulmonary function tests
Few of the numerous pulmonary function tests currently available impact upon clinical management of the critically ill, particularly if the patient has to be moved to a laboratory. A number of other tests require highly specialised equipment and fulfil a predominant research role.

Clinically relevant tests

Measurement	Test	Common clinical use
PaO_2, SaO_2, $PaCO_2$	Arterial blood gases	
SpO_2	Pulse oximetry	
End-tidal PCO_2	Capnography	
Vital capacity, tidal volume	Spirometry, electronic flowmetry	Serial measurement of borderline function (VC <10–15ml/kg) e.g. Guillain–Barré syndrome
Peak expiratory flow rate FEV_1, FVC	Wright peak flow meter Spirometry, electronic flowmetry	(Spontaneous ventilation) asthma (Spontaneous ventilation) asthma, obstructive/restrictive disease
Lung/chest wall compliance (see equations opposite)	Pressure–volume curve	Ventilator adjustments, monitoring disease progression
Flow-volume loop, pressure-volume loop	Pneumotachograph manometry	Ventilator adjustments

Research tests (examples)

Measurement	Test	Research use
Diaphragmatic strength (transdiaphragmatic pressure)	Gastric and oesophageal manometry	Respiratory muscle function, weaning
Pleural (intrathoracic) pressure	Oesophageal manometry	Ventilator trauma, work of breathing, weaning
Functional residual capacity	Closed circuit helium dilution, (bag-in-a-box) open circuit N_2 washout	Lung volumes, compliance
Ventilation–perfusion relationship	Multiple inert gas elimination technique, isotope techniques	Regional lung ventilation–perfusion, pulmonary gas exchange
Pulmonary diffusing capacity	Carbon monoxide uptake	Pulmonary gas exchange

Notes

- Compliance equals the change in pressure during a linear increase of 1l in volume above FRC.
- The alveolar–arterial oxygen difference is <2kPa in youth and <3.3kPa in old age.
- The Bohr equation calculates physiological deadspace, V_D. The normal value is below 30%.
- The shunt equation estimates the proportion of blood shunted past poorly ventilated alveoli (Q_S) compared to total lung blood flow (Q_T).

  These equations allow estimation of ventilation/perfusion mismatch:

- V/Q=1, ventilation and perfusion are well-matched.
- V/Q>1, increased deadspace (where alveoli are poorly perfused but well ventilated).
- V/Q<1, increased venous admixture or shunt (where alveoli are perfused but poorly ventilated).
- The normal range is <15%.

Lung volumes and capacity

TLC = total lung capacity
VC = vital capacity
FRC = functional residual capacity
TV = tidal volume
RV = residual volume

Figure. No Caption Available.
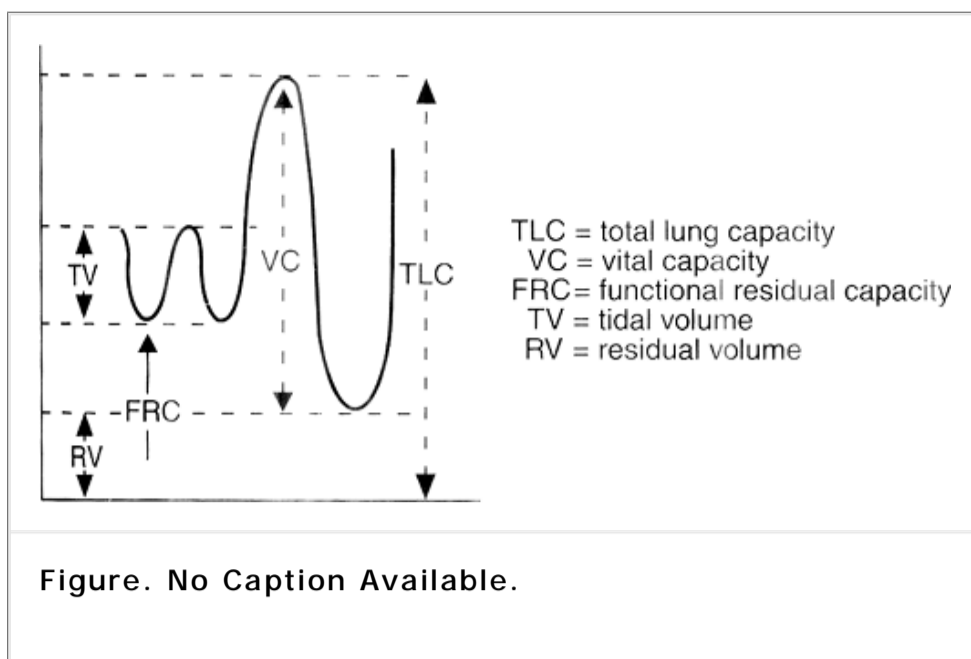
Equations

Alveolar gas equation

$P_AO_2 = FIO_2 - (PaCO_2/\text{respiratory quotient})$ [RQ often approximated to 0.8]

Alveolar-arterial oxygen difference

(A-a) difference = $FIO_2 \times 94.8 - PaCO_2 - PaO_2$

Bohr equation:

$V_D/V_T = (PaCO_2 - \text{expired } PCO_2)/PaCO_2$

Shunt equation

$Q_S/Q_T = (CcO_2 - CaO_2)/(CcO_2 - CvO_2)$

where CcO_2 = end-capillary O_2 content, a = arterial, v = mixed venous

See also:

Ventilatory support—indications; IPPV—adjusting the ventilator; IPPV—weaning techniques; IPPV—assessment of weaning; Pulse oximetry; CO_2 monitoring; Blood gas analysis; Chronic airflow limitation; Asthma—general management; Asthma—ventilatory management; Acute weakness; Guillain–Barré syndrome; Myasthenia gravis; Rheumatic disorders; Vasculitides

Pressure–volume relationship

This is determined by the compliance of the lungs and chest wall. The inspiratory pressure–volume relationship contains three components: an initial increase in pressure with no significant volume change; a linear increase in volume as pressure increases (the slope of which represents respiratory system compliance); and a further period of pressure increase with no volume increase. These three phases are separated by two inflexion zones, the lower representing the opening pressure of the system after flow resistance has been overcome in smaller airways and the upper approximating to total lung capacity. The expiratory pressure–volume relationship should normally approximate the inspiratory curve, returning to functional residual capacity. In patients with small airway collapse, separation of the inspiratory and expiratory curves occurs (hysteresis) as gas is trapped in smaller airways at the end of expiration.

Dynamic measurement

A pressure–volume loop may be viewed on most modern mechanical ventilators. A square wave inspiratory waveform (constant flow) and no inspiratory pause are necessary for waveform interpretation.

Static measurement

Small incremental lung volumes (200ml) are delivered with a calibrated syringe. The pressure measurement after each increment is taken under zero flow conditions, allowing construction of a pressure–volume curve. A quasistatic curve can be constructed by setting incremental tidal volumes (e.g. between 100 and 1000ml) for successive ventilator breaths and measuring the pressure during an inspiratory pause.

Use of pressure volume curves

Since respiratory muscle activity can alter intrathoracic pressure, the pressure volume curve is more easily obtained in the relaxed, fully ventilated patient. Both static and dynamic respiratory system compliance can be determined as the slope of the linear portion of the curve, i.e. where incremental pressure inflates the lungs. Below the lower inflexion zone the small airways are closed and expiration does not reach functional residual capacity. The lower inflexion zone therefore represents the appropriate setting for external PEEP to avoid gas trapping. Above the upper inflexion zone the lungs cannot inflate further. The upper inflexion zone therefore represents the maximum setting for

peak airway pressure.

Compliance: calculations

Lung compliance $(l/cmH_2O) = \Delta V_L/\Delta P_L$ where L, the litre above FRC, is the slope of the linear portion of the curve.

Total respiratory system compliance is derived from the equation:

(1/total compliance) = (1/lung compliance) + (1/chest wall compliance)

Total compliance can be calculated in well sedated, ventilated patients as:

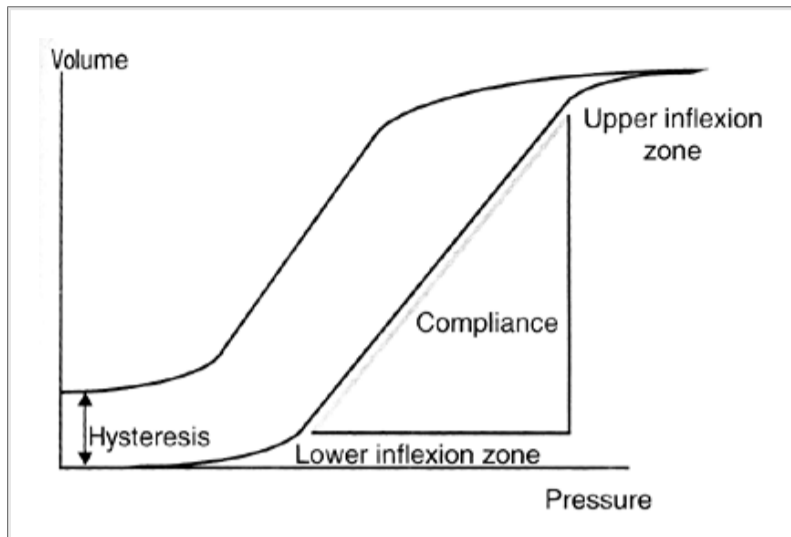tidal volume/(end-inspiratory pause pressure - PEEP).

Figure. No Caption Available.

See also:

Ventilatory support—indications; IPPV—adjusting the ventilator, p10; Positive end expiratory pressure (1), p22; Positive end expiratory pressure (2), p24; Chronic airflow limitation, p286; Asthma—general management, p286; Asthma—ventilatory management, p298

Blood gas machine

A small amount of heparinised blood is either injected from a syringe or aspirated from a capillary tube into the machine. The blood comes into contact with three electrodes which measure pH, PO_2 and PCO_2.

- pH—measured by the potential across a pH-sensitive glass membrane separating a sample of known pH and the test sample.

- PO_2—the partial oxygen pressure, is measured by applying a polarising voltage between a platinum cathode and a silver anode (Clark electrode). O_2 is reduced, generating a current proportional to the PO_2.

- PCO_2—the partial pressure of carbon dioxide, utilises a pH electrode with a Teflon membrane (Severinghaus electrode) which allows through uncharged molecules (CO_2) but not charged ions (H^+). CO_2 alone thus changes the pH of a bicarbonate electrolyte solution, the change being linearly related to the PCO_2.

- Hb—estimated photometrically; this is not as accurate as co-oximetry (see below).

- Bicarbonate—calculated by the Henderson–Hasselbach equation

$$pH = 6.1 + Log_{10}\frac{arterial\ [HCO_3^-]}{PaCO_2 \times 0.03}$$

  Actual HCO_3^- includes bicarbonate, carbonate and carbamate.

- Actual base excess (deficit)—the difference in concentration of strong base (acid) in whole blood and that titrated to pH 7.4, at PCO_2 5.33kPa and 37°C.

- Standard base excess (deficit)—a calculated *in vivo* base excess (deficit).

- Standard bicarbonate—the plasma concentration of hydrogen carbonate equilibrated at PCO_2 5.33kPa, PO_2 13.33kPa and temperature 37°C.

Blood gas values can be given either as 'pHstat' or 'alphastat', the former correcting for body temperature by shifting the calculated Bohr oxyhaemoglobin dissociation curve (hyperthermia to the right, hypothermia to the left). Alphastat measures true blood gas levels in the sample.

Co-oximeter

This differs from a blood gas machine in that the blood is haemolysed to calculate (i) total Hb and fetal Hb and (ii) oxyHb, carboxyhaemoglobin (COHb), methaemoglobin and sulphaemoglobin by utilising absorbance at six wavelengths (535, 560, 577, 622, 636, 670nm).

Taking a good blood gas sample

Use a 1ml syringe containing preferably a dry heparin salt (if not, liquid sodium heparin 1000iu/ml solution just filling the hub). Take sample, expel air, mix sample thoroughly and insert without delay.

Cautions

- Too much heparin causes dilution errors and is acidic.
- Nitrous oxide or halothane anaesthesia may give unreliable PO_2 values.
- Intravenous lipid administration may affect pH values.
- Abnormal (high/low) plasma protein concentrations affect base deficit.

See also:

Blood gas analysis, p100; Invasive blood gas monitoring, p102

Blood gas analysis

A heparinised (arterial, venous, capillary) blood sample can be inserted into a blood gas machine and/or co-oximeter for measurement of gas tensions and saturations, and acid–base status.

Measurements

- Identification of arterial hypoxaemia and hyperoxia, hypercapnia and hypocapnia—enabling monitoring of disease progression and efficacy of treatment. Ventilator and FIO_2 adjustments can be made precisely.
- pH, $PaCO_2$ and base deficit (or bicarbonate) values can be reviewed in parallel for diagnosis of acidosis and alkalosis, whether it is respiratory or metabolic in origin, and whether any compensation has occurred. (See figure opposite).
- Using a co-oximeter, accurate measurement can be made of haemoglobin oxygen saturation and also the total Hb level. The more sophisticated co-oximeters permit measurement of the fraction of metHb, COHb, deoxyHb and fetal Hb.
- Measurement of mixed venous oxygen saturation—for calculation of oxygen consumption and monitoring of oxygen supply:demand balance.

Causes of acid–base disturbances

- Respiratory acidosis—excess CO_2 production and/or inadequate excretion, e.g. hypoventilation, excess narcotic
- Respiratory alkalosis—reduction in $PaCO_2$ due to hyperventilation
- Metabolic acidosis—usually lactic, keto, renal or tubular. Consider tissue hypoperfusion, ingestion of acids (e.g. aspirin), loss of alkali (e.g. diarrhoea, renal tubular acidosis), diabetic ketoacidosis and hyperchloraemia (e.g. from excess normal saline administration)
- Metabolic alkalosis. Consider excess alkali (e.g. bicarbonate or buffer infusion), loss of acid (e.g. large gastric aspirates, renal), hypokalaemia, drugs (e.g. diuretics)

Normal values

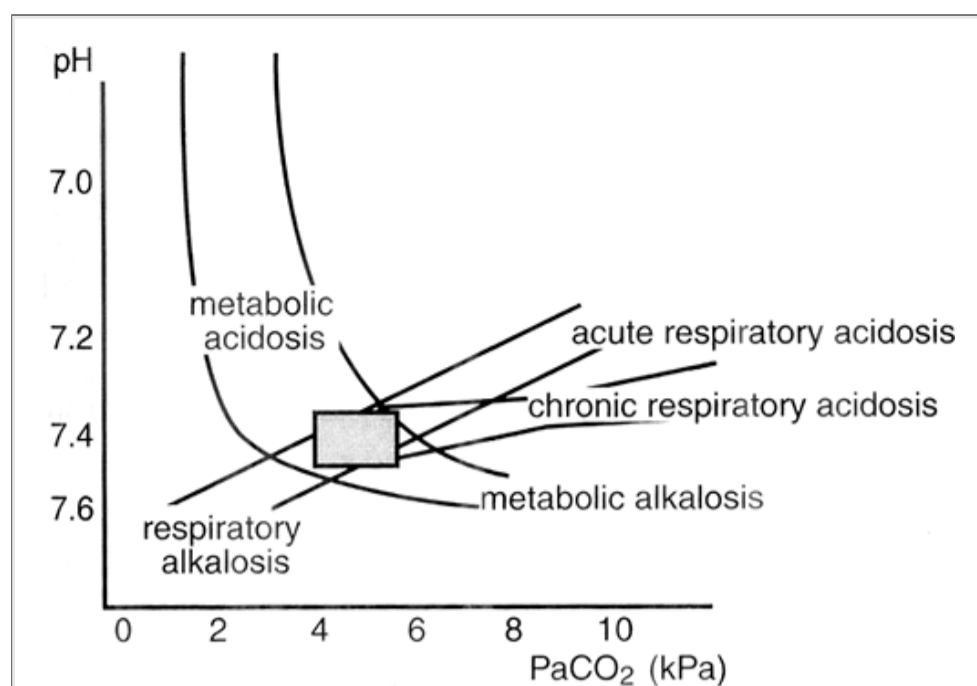|	
pH	7.35–7.45
PCO_2	4.6–6kPa
PO_2	10–13.3kPa
HCO_3^-	22–26mmol/l
ABE	-2.4 to +2.2
Arterial O_2 saturation	95–98%
Mixed venous oxygen saturation	70–75%

Figure. No Caption Available.

See also:

Oxygen therapy, p2; Ventilatory support—indications, p4; IPPV—adjusting the ventilator, p10; IPPV— assessment of weaning, p18; Positive end expiratory pressure (1), p22; Positive end expiratory pressure (2), p24; Continuous positive airway pressure, p26; Non-invasive respiratory support, p32; Extracorporeal respiratory support, p34; Haemo(dia)filtration (1), p62; Haemo(dia)filtration (2), p64; Peritoneal dialysis, p66; Parenteral nutrition, p82; Blood gas machine, p98; Invasive blood gas monitoring, p102; Arterial cannulation, p112; Pulmonary artery catheter— use, p118; Gut tonometry, p130; Lactate, p170; Basic resuscitation, p270; Respiratory failure, p282; Chronic airflow limitation, p286; Acute chest infection (1), p288; Acute chest infection (2), p290; Acute respiratory distress syndrome (1), p292; Acute respiratory distress syndrome (2), p294; Asthma—general management, p296; Asthma—ventilatory management, p298; Heart failure—assessment, p324; General acid–base management, p432; Metabolic acidosis, p434; Metabolic alkalosis, p436; Diabetic ketoacidosis, p442; Poisoning—general principles, p452 Salicylate poisoning, p454; Inhaled poisons, p466; Post-operative intensive care, p534

Invasive blood gas monitoring

Continuous blood gas monitoring can be achieved via an intra-arterial heparin-bonded catheter with on-line display of directly measured and computed blood gas variables. Results are updated every 20–30s. Recalibration is generally recommended at 12-hrly intervals.

Technology

- Systems utilise either electrode, tonometric or optode technology.

- Electrode technology is similar to that described for blood gas machine measurement. Optical sensors utilise either absorbance or fluorescence spectrophotometry to measure the signal from the chemical interaction between the analyte (O_2, CO_2 and H^+) and an indicator phase.

Problems

- Damping of the arterial pressure waveform can occur through the presence of the catheter within the arterial cannula. A dedicated, non-tapering 20G cannula reduces this damping effect.

- An increasing drift in accuracy is recognised after several days.

See also:

Blood gas analysis, p100

Extravascular lung water measurement

Standard methods of assessing pulmonary oedema are indirect. The CXR allows qualitative assessment only and is slow to change in response to clinical treatment. Assessment of cardiac filling pressures does not take into account the degree of capillary permeability or lymphatic adaptation. Consequently, a relatively low CVP or PAWP may be associated with pulmonary oedema formation and high filling pressures in chronic heart failure may be associated with no oedema and be entirely appropriate. Extravascular lung water (EVLW) measurement provides a technique for quantifying pulmonary oedema and monitoring the response to treatment.

Measurement technique

The normal value of 4–7ml/kg for extravascular lung water has been derived by gravimetric techniques performed post-mortem. A double indicator technique may be used in living patients. Two indicators are injected via a central vein; one distributes within the vascular space and the other throughout the intra- and extravascular space. The volume of distribution of the indicators is derived from the dilution curves detected at the femoral artery. Cooled 5% glucose is used as a thermal indicator for intra- and extravascular volume and indocyanine green bound to albumin as a colorimetric indicator for intravascular volume. Detection at the femoral artery is by a fibreoptic catheter with a thermistor tip. The cardiac output is measured by thermodilution at the femoral artery. The rate of exponential decay of the thermodilution curve allows the derivation of the volume of distribution between the injection and detection sites (the heart and lungs).

Pulmonary thermal volume = thermodilution CO × rate of exponential decay of thermodilution curve (intra- and extravascular volume)

Similar principles may be applied to the dye dilution curve produced on injection of indocyanine green which is assumed to distribute within the vascular space only.

Pulmonary blood volume = dye dilution CO × rate of exponential decay of dye dilution curve (intravascular volume)

EVLW may be calculated by subtracting pulmonary blood volume from pulmonary thermal volume.

Limitations of EVLW measurement

Since it is known that albumin can exchange across capillary membranes, pulmonary blood volume is overestimated by this technique and extravascular lung water is therefore underestimated. However, the corresponding error is small and not particularly significant clinically. A more serious drawback is in the limitation of treatment options. Treatment of pulmonary oedema by diuresis and ultrafiltration has been shown to be less effective at reducing EVLW in capillary leak, compared to congestive heart failure. Similarly, the strategy of preventing oedema formation by diuresis while maintaining the circulation with catecholamine infusions appears to be futile; vasoconstriction so produced increases EVLW.

See also:

Cardiovascular Monitoring

ECG monitoring

Continuous ECG monitoring is routine in every intensive care unit. The standard technique is to display a three lead ECG (commonly lead II). Other limb leads may be used although the electrodes are placed at the shoulders and left side of the abdomen. Other lead configurations can be used for specific purposes:

Chest–Shoulder–V5	Early detection of left ventricular strain
Chest–Manubrium–V5	Early detection of left ventricular strain
Chest–Back–V5	P wave monitoring

Modern, continuous monitors include alarm functions for bradycardia and tachycardia monitoring, and software routines for arrhythmia detection or ST segment analysis.

Causes of changes in heart rate or rhythm

Changes in heart rate or rhythm may be an indication of:

Sympathetic activity

Circulatory insufficiency

Pain

Anxiety

Hypoxaemia

Hypercapnia

Adverse drug effects

Antiarrhythmics

Sedatives

Electrolyte imbalance

Fever

See also:

Blood pressure monitoring

Non-invasive techniques
Non-invasive techniques are intermittent but automated. They include oscillotonometry (detection of cuff pulsation as the systolic pressure), detection of arterial turbulence under the cuff, ultrasonic detection of arterial wall motion under the cuff and detection of blood flow distal to the cuff. Any cuff system should use a cuff large enough to cover two-thirds of the surface of the upper arm.

Invasive (direct) arterial monitoring
Blood pressure is most usefully monitored from larger limb arteries, e.g. femoral or brachial. However, the potential for damage to these arteries is considerable and most consider it safer to use the radial or dorsalis pedis arteries, the pressure in which is higher. The arterial cannula is connected to an appropriate transducer system via a short length of non-compliant manometer tubing. The transducer should be matched to the monitor, i.e. as recommended by the manufacturer of the monitor. The transducer must be zeroed to atmospheric pressure. The transducer should be positioned at the level of the 4th intercostal space in the mid-axillary line. The transducer, manometer tubing and cannula should be continuously flushed with 3ml/h heparinised saline (1000IU/l).

Damping errors
It is important that the monitoring system is correctly damped. An underdamped system will overestimate systolic and underestimate diastolic blood pressure. The converse is true for an overdamped system. Moreover, it is not possible to correctly interpret waveform shape if damping is not correct. A correctly damped system will return immediately to the pressure waveform after flushing. Return is slow in an overdamped system and there is often resonance around the baseline before return to the pressure waveform in an underdamped system.

Interpretation of waveform
The shape of the arterial pressure waveform gives useful qualitative information about the state of the heart and circulation:

Short systolic time

Hypovolaemia

High peripheral resistance

Marked respiratory swing

Hypovolaemia

Pericardial effusion

Airways obstruction

High intra-thoracic pressure

Slow systolic upstroke

Poor myocardial contractility

High peripheral resistance

Limitations of blood pressure monitoring

It is important not to rely on arterial blood pressure monitoring alone in the critically ill. A normal blood pressure does not guarantee adequate organ blood flow. Conversely, a low blood pressure may be acceptable if perfusion pressure and blood flow is adequate for all organs. Measurement of cardiac output, in addition to blood pressure, is necessary where there is doubt about the adequacy of the circulation.

Examples of arterial waveform shape
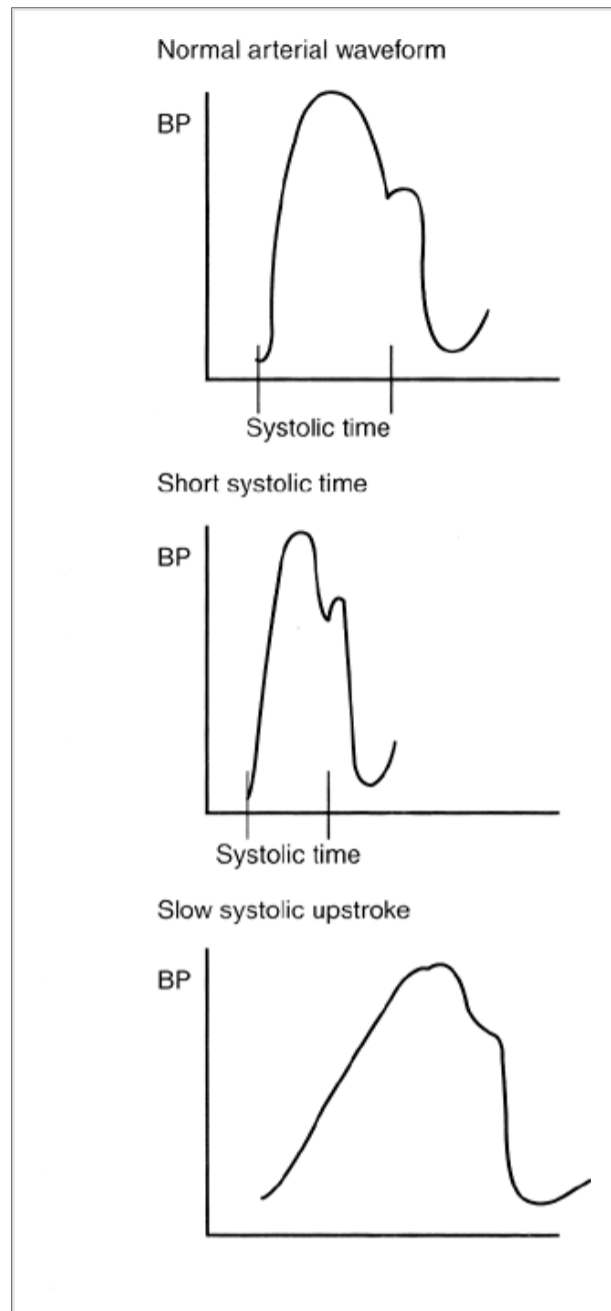
Figure. No Caption Available.

See also:
Arterial cannulation, p112; Hypotension, p312; Hypertension, p314

Arterial cannulation

Indications
Performed correctly, arterial cannulation is a safe technique allowing continuous monitoring of blood pressure and frequent sampling of blood. It is indicated in any patient with unstable or potentially unstable haemo-dynamic or respiratory status.

Radial artery cannulation
The radial artery is most frequently chosen because it is accessible and has good collateral blood flow. Allen's test, used to confirm the ulnar arterial blood supply, is not reliable.

Technique of cannulation
The wrist is hyperextended and the thumb abducted. After skin cleansing local anaesthetic (1% plain lidocaine) is injected into the skin and subcutaneous tissue over the most prominent pulsation. The course of the artery is noted and a 20G Teflon cannula is inserted along the line of the vessel. The usual technique is to enter the vessel in the same way as an intravenous cannula would be inserted. There is usually some resistance to skin puncture. To avoid accidentally puncturing the posterior wall of the artery, the skin and artery should be punctured as two distinct manoeuvres. Alternatively, a small skin nick may be made to facilitate skin entry.

In the case of elderly patients with mobile, atheromatous vessels a technique that involves deliberate transfixation of the artery may be used. The cannula is passed through the anterior and posterior walls of the vessel, thus

immobilising it. The needle is removed and the cannula withdrawn slowly into the lumen vessel, before being advanced forward.

Seldinger-type kits are also available for arterial cannulation. A guidewire is first inserted through a rigid steel needle. The indwelling plastic cannula is then placed over the guidewire.

The cannula should be connected to a continuous flushing device after successful puncture. Flushing with a syringe should be avoided since the high pressures generated may lead to a retrograde cerebral embolus.

Alternative sites for cannulation

Brachial artery
End artery supplying a large volume of tissue. Thus thrombosis has potentially severe consequences.

Ulnar artery
Should be avoided if the radial artery is occluded.

Femoral artery
May be difficult to keep clean. Also supplies a large volume of tissue. A longer catheter should be used to avoid displacement.

Dorsalis pedis artery
Blood pressure will be at least 10–20mmHg higher than in the central circulation.

Complications

- Digital ischaemia due to arterial spasm, thrombosis or embolus
- Bleeding in cases with altered coagulation status
- Infection is a risk in prolonged cannulation
- False aneurysm

See also:
Blood gas analysis, p100; Invasive blood gas monitoring, p102; Blood pressure monitoring, p110; Routine changes of disposables, p478

Central venous catheter—use

Types of catheter

- Single, double, triple or quadruple lumen.
- Sheaths for insertion of pulmonary artery catheter or pacing wire.
- Tunnelled catheter for long term use.
- Multilumen catheters allow multiple infusions to be given separately ± continuous pressure monitoring. Minimises accidental bolus risk.
- Large-bore double lumen catheters used for venovenous dialysis/filtration.
- Common routes are internal jugular, subclavian and femoral.
- 'Long' catheters can be inserted via brachial or axillary veins though are generally not used due to the risk of thrombosis.

Uses

- Invasive haemodynamic monitoring.
- Infusion of drugs that can cause peripheral phlebitis or tissue necrosis if tissue extravasation occurs (e.g. TPN, epinephrine, amiodarone).
- Rapid volume infusion. NB the rate of flow is inversely proportional to the length of the cannula.
- Access, e.g. for pacing wire insertion.
- Emergency access when peripheral circulation is 'shut down'.
- Renal replacement therapy, plasmapheresis, exchange transfusion.

Contraindications/cautions

- Coagulopathy.

- Undrained pneumothorax on contralateral side.

- Agitated, restless patient.

Complications

- Arterial puncture.

- Haemorrhage.

- Arrhythmias.

- Infection (usually skin, occasionally sepsis or endocarditis).

- Pneumothorax.

- Air embolism, venous thrombosis, haemothorax, chylothorax (rare).

Central venous pressure measurement

Use of an electronic pressure transducer is preferable to manometry which incorporates a three-way tap, a fluid reservoir bag and a fluid-filled vertical column, the height of which corresponds to CVP. The pressure transducer should be placed and 'zeroed' at the level of the left atrium (approximately mid-axillary line) rather than the sternum which is more affected by patient position (supine/semi-erect/prone). Venous pulsation and some respiratory swing should be seen in the trace but not a RV pressure waveform (i.e. catheter inserted too far).

Troubleshooting

Excessive bleeding at the insertion site is usually controlled by direct compression. If not controlled, correct any coagulopathy, If post-thrombolysis, consider tranexamic acid.

The incidence of local infection (usually coagulase negative Staphylococci or *S. aureus*) rises after 5 days. Routine change of catheter at 5–7 days is not necessary though change over a wire may be sufficient if the patient develops an unexplained pyrexia or neutrophilia. However, removal ± change of site is needed if the site is cellulitic or blood cultures taken through the catheter are positive.

See also:

Central venous catheter—insertion

Ultrasound-guided placement should be considered, especially for difficult placements. The technique with ultrasound guidance is different from the landmark technique; operators should to be able to identify a patent vein and manipulate both probe and cannula simultaneously. There will be many situations where an ultrasound device may be unavailable so placement using anatomical landmarks alone should still be learnt.

Landmarks

Various landmarks have been described. For example:

- Internal jugular: Halfway between mastoid process and sternal notch, lateral to carotid pulsation and medial to medial border of sternocleidomastoid. Aim toward ipsilateral nipple, advancing under body of sternocleidomastoid until vein entered.

- Subclavian: 3 cm below junction of lateral third and medial two thirds of clavicle. Turn head to contralateral side. Aim for point between jaw and contralateral shoulder tip. Advance needle subcutaneously to hit clavicle. Scrape needle under clavicle and advance further until vein entered.

- Femoral: Locate femoral artery in groin. Insert needle 3cm medially and angled rostrally. Advance until vein entered.

Insertion technique

The Seldinger technique (described below) is safer than the 'catheter-over-needle' technique and should generally be used in ICU patients.

1. Use aseptic technique throughout. Clean area with antiseptic and surround with sterile drapes. Anaesthetise local area with 1% lidocaine. Flush lumen(s) of catheter with saline.

2. Use metal needle to locate central vein.

3. Pass wire (with 'J' or floppy end leading) through needle into vein. Only minimal resistance at most should be felt. If not, remove wire and confirm needle tip is still located within vein lumen. Monitor for arrhythmias. If

these occur, wire is probably at tricuspid valve. Usually responds to retracting wire a few cm.

4. Remove needle leaving wire extruding from skin puncture site.

5. Depending on size/type of catheter to be inserted, a rigid dilator (± preceded by a scalpel incision to enlarge puncture site) may be passed over the wire to form a track through the subcutaneous tissues to the vein. Remove dilator.

6. Thread catheter over wire. Ensure end of wire extrudes from catheter to prevent accidental loss of wire in vein. Insert catheter into vein to depth of 15–20cm. Remove wire.

7. Check for flashback of blood down each lumen and respiratory swing, then flush with saline.

8. Suture catheter to skin. Clean and dry area. Cover with sterile transparent semipermeable dressing.

9. A CXR is usually performed to verify correct position of tip (junction of superior vena cava and right atrium) and to exclude a pneumothorax. Unless in an emergency situation, a satisfactory position should generally be confirmed before use of the catheter.

Pulmonary artery catheter—use

Though in clinical use for 30 years, retrospective data analyses suggested an association between catheter use and increased mortality that has not been confirmed by prospective trials. Studies have also found an inadequate knowledge base regarding insertion and data interpretation so proper training in its use is mandated.

Uses

- Pressure monitoring—RA, RV, PA, PAWP
- Flow monitoring—(right ventricular) cardiac output
- Oxygen saturation—'mixed venous' (i.e. in RV outflow tract/PA), determination of left to right shunts (ASD, VSD)
- Derived variables—SVR, PVR, LVSW, RVSW, DO_2, VO_2, O_2ER
- Temporary pacing
- Right ventricular ejection fraction and end-diastolic volume

Specialised catheters

- Continuous mixed venous oxygen saturation measurement
- Continuous cardiac output measurement
- RV end-diastolic volume, RV ejection fraction calculation
- Ventricular (±atrial) pacing

Management

Monitor PA pressure continuously to recognise forward catheter migration and pulmonary arterial occlusion. If so, correct immediately by partial catheter withdrawal to prevent infarction.

The risk of local infection (usually *Staph. aureus* or coagulase negative staphylococci) rises after 5 days. A catheter change over a guidewire may be sufficient if unexplained pyrexia or neutrophilia develops. Removal ± change of site is needed if the site is cellulitic, or positive cultures are grown from either line tip or blood.

Withdraw samples of pulmonary artery blood slowly from the distal lumen to prevent 'arterialization', i.e. pulmonary venous sampling.

Wedge pressure measurements

Inflate balloon slowly, monitoring the waveform to avoid overwedging and potential vessel rupture especially if elderly and/or pulmonary hypertensive. The trace should only 'wedge' after ≥1.3ml air has been injected.

Measure at end-expiration when intrathoracic pressure is closest to atmospheric pressure. For ventilated patients end expiration ≡ lowest wedge reading; during spontaneous breathing end expiration ≡ highest reading. Measurement is difficult in the dyspnoeic patient; a 'mean' wedge reading may be used in this instance.

The PAWP cannot be higher than the PA diastolic pressure.

CVP, PAWP and CO should not be measured during rapid volume infusion but after a period of equilibration (5-10 min).

The PAWP does not equal the LVEDP in mitral stenosis.

In mitral regurgitation measure PAWP at the end of the 'A' wave.

West's zones

The catheter tip should lie in a zone III region where PA pressure >PV pressure >alveolar pressure and below left

atrial level on a lateral CXR.

Suspect a non-zone III position if (i) following a rise in PEEP, the PAWP rises by >50% of the increment, (ii) the wedge trace shows no detectable cardiac pulsation and/or excess respiratory variation.

A non-zone III position is more likely with PEEP and/or hypovolaemia.

Normal values

Stroke volume	70–100ml
Cardiac output	4–6l/min
Right atrial pressure	0–5mmHg
Right ventricular pressure	20–25/0–5mmHg
Pulmonary artery pressure	20–25/10–15mmHg
Pulmonary artery wedge pressure	6–12mmHg
Mixed venous oxygen saturation	70–75%

Derived variables

Variable	Calculation	Normal range
Cardiac index (CI)	$\dfrac{CO}{Body\ surface\ area}$	$2.5–3.5l/min/m^2$
Stroke index (SI)	$\dfrac{SV}{Body\ surface\ area}$	$40–60ml/m^2$
Systemic vascular resistance	$\dfrac{MAP - RAP \times 79.9}{CO}$	$960–1400dyns/cm^5$
Pulmonary vascular resistance	$\dfrac{PAP - PAWP \times 79.9}{CO}$	$25–125dyns/cm^5$
Left ventricular stroke work index	$(MAP–PAWP) \times SI \times 0.0136$	$44–68g\text{-}mm^2$
Right ventricular stroke work index	$(MPAP–RAP) \times SI \times 0.0136$	$4–8g\text{-}mm^2$
Oxygen delivery	$0.134 \times CO \times Hb_a \times SaO_2$	950–1300ml/min
Oxygen consumption	$0.134 \times CO \times (Hb_a \times SaO_2 - Hb_v \times SvO_2)$	180–320ml/min
Oxygen extraction ratio	$1 - \dfrac{SaO_2 - SvO_2}{SaO_2}$	0.25–0.30

Key trials and studies

Connors AF Jr et al. The effectiveness of right heart catheterization in the initial care of critically ill patients. JAMA 1996; 276:889–97

Richard C et al. Early use of the pulmonary artery catheter and outcomes in patients with shock and acute respiratory distress syndrome: a randomized controlled trial. JAMA 2003; 290:2713–20

Iberti TJ et al. A multicenter study of physicians' knowledge of the pulmonary artery catheter. JAMA 1990; 264:2928–32

See also:

Positive end expiratory pressure (1), p22; Positive end expiratory pressure (2), p24; Blood gas analysis, p100; Extravascular lung water measurement, p104; Central venous catheter—use, p114; Central venous catheter—insertion, p116; Pulmonary artery catheter—insertion, p120; Cardiac output—thermodilution, p122; Cardiac output—other invasive, p124; Fluid challenge, p274; Heart failure—assessment, p324; Routine changes of disposables, p478

Pulmonary artery catheter—insertion

Insertion

1. Insert 8Fr central venous introducer sheath under strict aseptic technique. Pulmonary artery catheterisation is easier via internal jugular or subclavian veins.

2. Prepare catheter pre-insertion—3-way taps on all lumens, flush lumens with crystalloid, inflate balloon with 1.6ml air and check for concentric inflation and leaks, place transparent sleeve over catheter to maintain future sterility, pressure transduce distal lumen and zero to a reference point (usually mid-axillary line). Depending on catheter type, other pre-insertion calibration steps may be required, e.g. oxygen saturation.

3. Insert catheter 15cm (i.e. beyond the length of the introducer sheath) before inflating balloon. Advance catheter smoothly through the right heart chambers. Pause to record pressures and note waveform shape in RA, RV and PA. When a characteristic PAWP waveform is obtained, stop advancing catheter, deflate balloon and ensure that PA waveform reappears. If not, withdraw catheter by a few cm.

4. Slowly re-inflate balloon, observing waveform trace. The wedge recording should not be obtained until at least 1.3ml of air has been injected into the balloon. If not, withdraw catheter 1–2cm and repeat. If 'overwedged' (pressure continues to climb on inflation), catheter is inserted too far and balloon has inflated forward over distal lumen. Immediately deflate, withdraw catheter 1–2cm and repeat.

5. After insertion, a CXR is usually performed to verify catheter position and to exclude pneumothorax.

Contraindications/cautions

- Coagulopathy
- Tricuspid valve prosthesis or disease

Complications

- Problems of central venous catheterisation
- Arrhythmias (especially when traversing tricuspid valve)
- Infection (including endocarditis)
- Pulmonary artery rupture
- Pulmonary infarction
- Knotting of catheter
- Valve damage (do not withdraw catheter unless balloon deflated)

Troubleshooting

Excessive catheter length in a heart chamber causes coiling and a risk of knotting. No more than 15–20cm should be passed before the waveform changes. If not, deflate balloon, withdraw catheter, repeat. A knot can be managed by (i) 'unknotting' with an intraluminal wire, (ii) pulling taut and removing catheter + introducer sheath together, or (iii) surgical or angiographic intervention.

If catheter fails to advance to next chamber, consider 'stiffening' catheter by injecting iced crystalloid through distal lumen, rolling patient to left lateral position or advancing catheter slowly with balloon deflated.

The catheter should never be withdrawn with the balloon inflated.

Arrhythmias on insertion usually occur when the catheter tip is at the tricuspid valve. These usually resolve on withdrawing the catheter or, occasionally, after a slow bolus of 1.5mg/kg lidocaine.
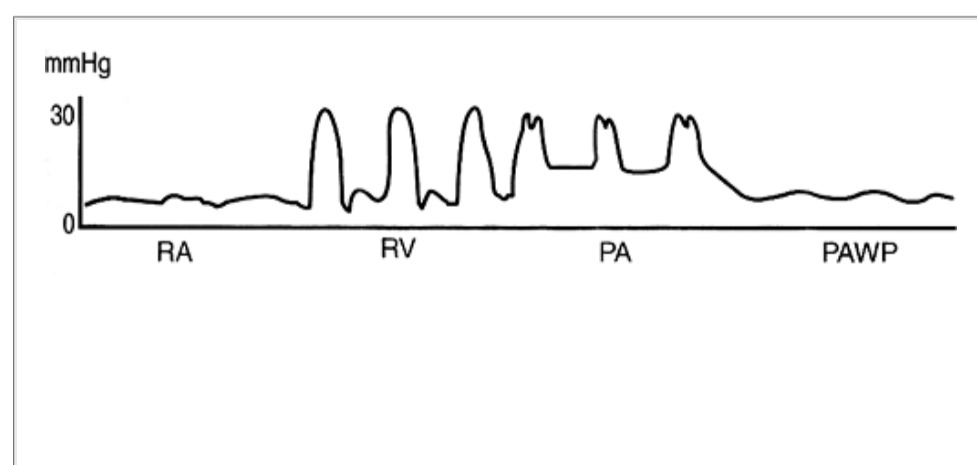
Waveforms

Cardiac output—thermodilution

Thermodilution is the technique utilised by the pulmonary artery catheter to measure right ventricular cardiac output. The principle is a modification of the Fick principle whereby a bolus of cooled 5% glucose is injected through the proximal lumen into the central circulation (right atrium) and the temperature change is detected by a thermistor at the catheter tip, some 30cm distal. A modification of the Hamilton–Stewart equation, utilising the volume, temperature and specific heat of the injectate, enables cardiac output to be calculated by an on-line computer from a curve measuring temperature change in the pulmonary artery.

Continuous thermodilution measurement uses a modified catheter that emits heat pulses from a thermal filament lying within the right ventricle and right atrium, 14–25cm from the tip. 7.5W of heat are added to the blood intermittently every 30–60s and these temperature changes are measured by a thermistor 4cm from the tip. Though updated frequently, the cardiac output displayed is usually an average of the previous 3–6min.

Thermodilution injection technique

The computer constant must be set for the volume and temperature of the 5% glucose used. 10ml of ice-cold glucose provides the most accurate measure. 5ml of room temperature injectate is sufficiently precise for normal and high output states however its accuracy does worsen at low output values.

1. Press 'Start' button on computer.

2. Inject fluid smoothly over 2–3s.

3. Repeat at least twice more at random points in the respiratory cycle.

4. Average 3 measurements falling within 10% of each other. Reject outputs gained from curves that are irregular/non-smooth.

Erroneous readings

- Valve lesions—tricuspid regurgitation will allow some of the injectate to reflux back into the right atrium. Aortic incompetence produces a higher left ventricular output as a proportion will regurgitate back into the left ventricle.

- Septal defects.

- Loss of injectate. Check that connections are tight and do not leak.

Advantages

- Most commonly used and familiar ICU technique, computer warnings of poor curves.

Disadvantages

- Non-continuous (by injection technique).

- 5–10% inter- and intraobserver variability.

- Erroneous readings with tricuspid regurgitation, intracardiac shunts.

- Frequently repeated measurements may result in considerable volumes of 5% glucose being injected.

Cardiac output—other invasive

Dye dilution

Mixing of a given volume of indicator to an unknown volume of fluid allows calculation of this volume from the degree of indicator dilution. The time elapsed for the indicator to pass some distance in the cardiovascular system yields a

cardiac output value, calculated as:

$$\frac{60 \times I}{C_m \times t}$$

...where I is the amount of indicator injected, C_m is the mean concentration of the indicator and t is the total duration of the curve. The traditional dye dilution technique is to inject indocyanine green into a central vein followed by repeated sampling of arterial blood to enable construction of a time—concentration curve with a rapid upstroke and an exponential decay. Plotting the dye decay curve semilogarithmically and extrapolating values to the origin produces the cardiac output. The COLD-Pulsion device measures the concentration decay directly from an indwelling arterial probe, thus computing cardiac output. Alternatively, this device may use the thermodilution approach, avoiding pulmonary artery catheterisation. The LiDCO device is based on a similar principle using lithium as the 'dye'.

Advantages
Reasonably accurate, less invasive than pulmonary artery catheter placement.

Disadvantages
Invasive, recirculation of dye prevents multiple repeated measurements, lengthy, underestimates low output values. Inaccurate with moderate/ severe valvular regurgitation. Use of paralysing agents may interfere with lithium measurement.

Direct Fick
The amount of substance passing into a flowing system is equal to the difference in concentration of the substance on each side of the system multiplied by the flow within the system. Cardiac output is thus usually calculated by dividing total body oxygen consumption by the difference in oxygen content between arterial and mixed venous blood. Alternatively, CO_2 production can be used instead of VO_2 as the indicator. Arterial CO_2 can be derived non-invasively from end-tidal CO_2 while mixed venous CO_2 can be determined by rapid rebreathing into a bag until CO_2 levels have equilibrated.

Advantages
'Gold standard' for cardiac output estimation.

Disadvantages
For VO_2: Invasive (requires measurement of mixed venous blood), requires leak-free open circuit or an unwieldy closed circuit technique. Oxygen consumption measurements via metabolic cart unreliable if FIO_2 is high. Lung oxygen consumption not measured by pulmonary artery catheter technique (may be high in ARDS, pneumonia...).

For CO_2: Non-invasive but requires normal lung function and is thus not generally applicable in ICU patients.

See also:

Cardiac output—non-invasive (1)

Doppler ultrasound
An ultrasound beam of known frequency is reflected by moving red blood corpuscles with a shift in frequency proportional to the blood flow velocity. The actual velocity can be calculated from the Doppler equation which requires the cosine of the vector between the direction of the ultrasound beam and that of blood flow. This has been applied to blood flow in the ascending aorta and aortic arch (via a suprasternal approach), descending thoracic aorta (oesophageal approach) and intracardiac flow (e.g. transmitral from an apical approach). Spectral analysis of the Doppler frequency shifts produces velocity—time waveforms, the area of which represents the 'stroke distance', i.e. the distance travelled by a column of blood with each left ventricular systole (see figure opposite). The product of stroke distance and aortic (or mitral valve) cross-sectional area is stroke volume. Cross-sectional area can be measured echocardiographically; however, as both operator expertise and equipment is required, this additional measurement can be either ignored or assumed from nomograms to provide a reasonable *estimate* of stroke volume.

Advantages
Quick, safe, minimally invasive, reasonably accurate, continuous (via oesophageal approach), other information on contractility, preload and afterload from waveform shape (see figure opposite).

Disadvantages
Non-continuous (unless via oesophagus), learning curve, operator dependent.

Echocardiography
Combines structural as well as dynamic assessment of the heart using ultrasound reflected off various interfaces. Transthoracic or transoesophageal probes provide information on valve integrity, global (diastolic and systolic) and

regional ventricular function, wall thickness, pericardial fluid or thickening, aortic dissection, ventricular volumes and ejection fraction, and pulmonary pressures. Often combined with integral Doppler ultrasound for cardiac output estimation derived from combined measurement of aortic diameter plus flow at various sites, e.g. left ventricular outflow tract, aorta, transmitral. Analytic software or formulae can also enable computation of cardiac output from estimations of ventricular volumes.

Advantages
Non-invasive, safe, relatively quick. Provides other useful information on cardiac structure and function.

Disadvantages
Expensive equipment, lengthy learning curve and interobserver variability. Body habitus or pathology (e.g. emphysema) may impair image quality.

Doppler blood flow velocity waveform variables

Figure. No Caption Available.
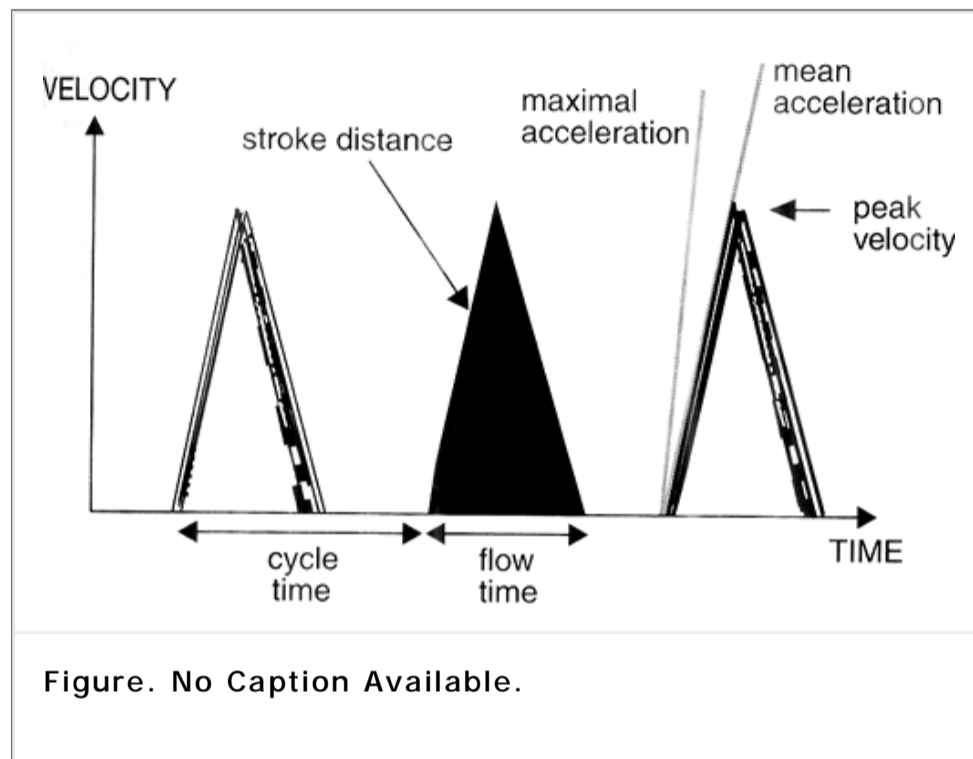
Changes in Doppler flow velocity waveform shape

Figure. No Caption Available.
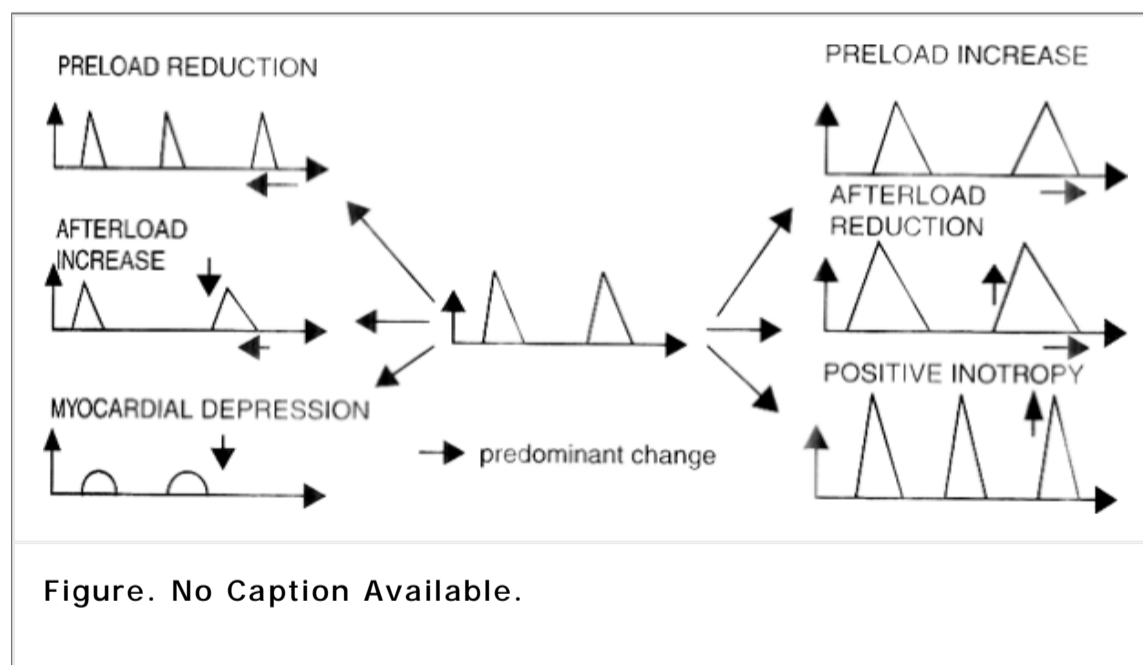
See also:
Cardiac output—thermodilution, p122; Cardiac output—other invasive, p124; Cardiac output—non-invasive (2), p128; Fluid challenge, p274; Hypotension, p312; Heart failure—assessment, p324; Systemic inflammation/multi-organ failure, p484; Burns—fluid management, p510

Cardiac output—non-invasive (2)

Pulse contour analysis
The concept of this technique is that the contour of the arterial pressure waveform is proportional to stroke volume. However, it is also influenced by aortic impedance so another cardiac output measuring technique (e.g. commercial devices utilising COLD-Pulsion or LiDCO) must be used in tandem for initial calibration. Although it can then be used as a means of continuous cardiac output monitoring, frequent re-calibration should be performed against the reference technique. This is particularly important when changes in impedance occur, e.g. with changes in cardiac

output, vascular tone, body temperature.

Advantages
Continuous flow monitoring, uses data from arterial cannula already *in situ* for pressure monitoring.

Disadvantages
Changes in vascular compliance will affect accuracy requiring frequent recalibration. Requires a good quality, non-obstructed and non-damped arterial waveform. There is debate about the relative quality of signal from radial vs. femoral artery.

Thoracic bioimpedance
Impedance changes originate in the thoracic aorta when blood is ejected from the left ventricle. This effect is used to determine stroke volume from formulae utilising the electrical field size of the thorax, baseline thoracic impedance and fluctuation related to systole, and ventricular ejection time. A correction factor for sex, height and weight is also introduced. The technique simply utilises four pairs of electrodes placed in proscribed positions on the neck and thorax; these are connected to a dedicated monitor which measures thoracic impedance to a low amplitude, high (70kHz) frequency 2.5mA current applied across the electrodes.

Advantages
Quick, safe, totally non-invasive, reasonably accurate in normal, spontaneously breathing subjects.

Disadvantages
Discrepancies in critically ill patients (especially those with arrhythmias, tachycardias, intrathoracic fluid shifts, anatomical deformities, aortic regurgitation), metal within the thorax, inability to verify signal.

See also:

Gut tonometry
A gas permeable silicone balloon attached to a sampling tube is passed into the lumen of the gut. Devices exist for tonometry in the stomach or sigmoid colon. The tonometer allows indirect measurement of the PCO_2 of the gut mucosa and calculation of the pH of the mucosa.

Indications
Gut mucosal hypoperfusion is an early consequence of hypovolaemia. Covert circulatory inadequacy due to hypovolaemia may be detected as gut mucosal acidosis and has been related to post-operative complications after major surgery. In critically ill patients there is some evidence that prevention of gut mucosal acidosis improves outcome. The sigmoid colon tonometer is useful to detect ischaemic colitis early (e.g. after abdominal vascular surgery).

Technique

Saline tonometry
In the original technique the tonometer balloon was prepared by degassing and filling with 2.5ml 0.9% saline. The saline was withdrawn into a syringe connected to the sampling tube prior to insertion. After insertion the saline was passed back into the balloon. The PCO_2 of the saline in the balloon equilibrated with the PCO_2 of the gut lumen over a period of 30–90min. At steady state it was assumed that the PCO_2 of the gut lumen and gut mucosa were in equilibrium. Time correction factors were derived for partial equilibration between the balloon saline and the gut lumen. The measurement was completed by sampling the saline from the balloon and an arterial blood sample for measurement of arterial $[HCO_3^-]$.

Gas tonometry
Using air in the tonometry balloon allows more rapid equilibration between the tonometer and the luminal PCO_2. A modified capnometer automatically fills the balloon with air and samples the PCO_2 after 5–10min equilibration. Subsequent cycles of balloon filling do not use fresh air so CO_2 equilibration is quicker. Tonometric PCO_2 may be compared with end-tidal PCO_2 (measured with the same capnometer) as an estimate of arterial PCO_2. With a normal capnogram, a balloon PCO_2 significantly higher than end-tidal PCO_2 implies gut mucosal hypoperfusion.

pH versus regional PCO_2
The pH of the gut mucosa (pHi) may be calculated using a modified Henderson–Hasselbach equation:

$$pHi = 6.1 + log_{10} \frac{arterial\ [HCO_3^-]}{PCO_2(tonometer) \times K}$$

where K is the time dependent equilibration constant. However, most of the variation in the measurement is due to variation in regional PCO_2. Comparing regional PCO_2 with $PaCO_2$ gives as much information as making the calculation

of pHi and overcomes the problematic assumption that arterial $[HCO_3^-]$ is equivalent to mucosal capillary $[HCO_3^-]$.

See also:

🟢 Ovid: Oxford Handbook of Critical Care

Neurological Monitoring

Intracranial pressure monitoring

Indications

To confirm the diagnosis of raised intracranial pressure (ICP) and monitor treatment. May be used in cases of head injury particularly if ventilated, Glasgow Coma Score ≤8, or with an abnormal CT scan. Also used in encephalopathy, post-neurosurgery and in selected cases of intracranial haemorrhage. Although a raised ICP can be related to poor prognosis after head injury, the converse is not true. Sustained reduction of raised ICP (or maintenance of cerebral perfusion pressure) in head injury may improve outcome although large controlled trials are lacking.

Methods of monitoring intracranial pressure

Ventricular monitoring

A catheter is inserted into the lateral ventricle via a burr hole. The catheter may be connected to a pressure transducer or may contain a fibreoptic pressure monitoring device. Fibreoptic catheters require regular calibration according to the manufacturer's instructions. Both systems should be tested for patency and damping by temporarily raising intracranial pressure (e.g. with a cough or by occluding a jugular vein). CSF may be drained through the ventricular catheter to reduce intracranial pressure.

Subdural monitoring

The dura is opened via a burr hole and a hollow bolt inserted into the skull. The bolt may be connected to a pressure transducer or admit a fibreoptic or hi-fidelity pressure monitoring device. A subdural bolt is easier to insert than ventricular monitors. The main disadvantages of subdural monitoring are a tendency to underestimate ICP and damping effects. Again calibration and patency testing should be performed regularly.

Complications

Infection—particularly after 5 days

Haemorrhage—particularly with coagulopathy or difficult insertion

Using ICP monitoring

Normal ICP is <10mmHg. A raised ICP is usually treated when >25mmHg in head injury. As ICP increases, there are often sustained rises in ICP to 50–100mmHg lasting for 5–20min, increasing with frequency as the baseline ICP rises. This is associated with a 60% mortality. Cerebral perfusion pressure (CPP) is the difference between mean BP and mean ICP. Treatment aimed at reducing ICP may also reduce mean BP. It is important to maintain CPP >50–60mmHg.

See also:

Jugular venous bulb saturation

Retrograde passage of a fibre-optic catheter from the internal jugular vein into the jugular bulb enables continuous monitoring of jugular venous bulb saturation (SjO_2). This can be used in conjunction with other monitors of cerebral haemodynamics such as middle cerebral blood flow, cerebral arteriovenous lactate difference and intracranial pressure to direct management.

Principles of SjO_2 management

Normal values are approximately 65–70%. In the absence of anaemia and with maintenance of normal SaO_2 values, values of SjO_2 >75% suggest luxury perfusion or global infarction with oxygen not being utilised; values <54% correspond to cerebral hypoperfusion while values <40% suggest global ischaemia and are usually associated with

increased cerebral lactate production. Knowledge of SjO_2 allows optimisation of brain blood flow to avoid (i) either excessive or inadequate perfusion and (ii) iatrogenically induced hypoperfusion through treating raised intracranial pressure aggressively with diuretics and hyperventilation. Studies in trauma patients have found (i) a higher mortality with episodes of jugular venous desaturation and (ii) a significant relationship between cerebral perfusion pressure (CPP) and SjO_2 when the CPP was <70mmHg. A falling SjO_2 may be an indication to increase CPP though no prospective randomised trial has yet been performed to study the effect on outcome.

Approximately 85% of cerebral venous drainage passes down one of the internal jugular veins (usually the right). SjO_2 usually represents drainage from both hemispheres and is equal on both sides; however, after focal injury, this pattern of drainage may alter.

Insertion technique

1. Insert introducer sheath rostrally in internal jugular vein.
2. Calibrate fibreoptic catheter pre-insertion.
3. Insert catheter via introducer sheath; advance to jugular bulb.
4. Withdraw introducer sheath.
5. Confirm (i) free aspiration of blood via catheter, (ii) satisfactory light intensity reading, (iii) satisfactory positioning of catheter tip by lateral cervical X-ray (high in jugular bulb, above level of 2nd cervical vertebra).
6. Perform *in vivo* calibration, repeat calibration 12-hrly.

Troubleshooting

If the catheter is sited too low in the jugular bulb, erroneous SjO_2 values may result from mixing of intracerebral and extracerebral venous blood. This could be particularly pertinent when cerebral blood flow is low.

Ensure light intensity reading is satisfactory; if too high the catheter may be abutting against a wall, and if low the catheter may not be patent or have a small clot over the tip. Before treating the patient, always confirm the veracity of low readings against a blood sample drawn from the catheter and measured in a co-oximeter.

Formulae

$$SjO_2\,(\%) = SaO_2\,(\%) - \frac{CMRO_2 \times 104}{CBF \times Hb \times 1.34}$$

where	SjO_2 = jugular bulb oxygen saturation
	$SaO_2(\%)$ = arterial oxygen saturation
	$CMRO_2$ = cerebral metabolism of oxygen
	CBF = cerebral blood flow

$$\text{cerebral oxygen extraction ratio} = \frac{SaO_2 - SjO_2}{SaO_2}$$

cerebral perfusion pressure = mean systemic BP - intracranial pressure

See also:

EEG/CFM monitoring

EEG monitoring

The EEG reflects changes in cortical electrical function. This, in turn, is dependent on cerebral perfusion and oxygenation. EEG monitoring can be useful to assess epileptiform activity as well as cerebral well-being in patients who are sedated and paralysed. The conventional EEG can be used intermittently but data reduction and artefact suppression are necessary to allow successful use of EEG recordings in the ICU.

Bispectral index (BIS) monitor

BIS is a statistical index derived from the EEG and expressed as a score between 0 and 100. Scores below 50 have been reliably associated with anaesthesia-induced unconsciousness. Assessment in the critically ill patient may be complicated by various confounding factors such as septic encephalopathy, head trauma and hypoperfusion. A low score is related to deep or excessive sedation, and may allow dose reduction (or cessation) of sedative agents, especially in paralysed patients.

Cerebral function monitor (CFM)

The CFM is a single channel, filtered trace from 2 recording electrodes placed over the parietal regions of the scalp. A third electrode may be used in the midline to help with interference detection. The parietal recording electrodes are usually placed close to watershed areas of the brain in order to allow maximum sensitivity for ischaemia detection. Voltage is displayed against time on a chart running at 6–30cm/h.
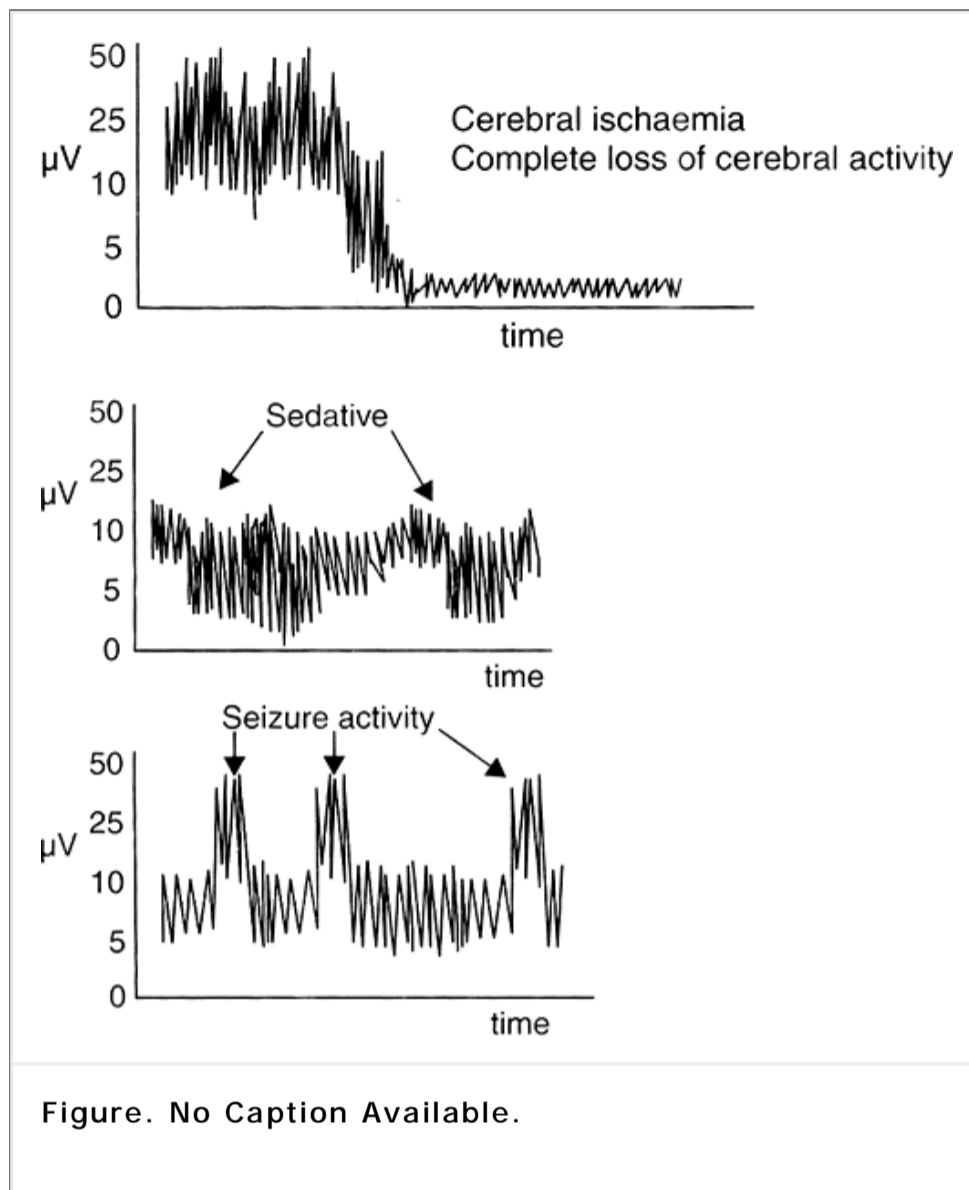
Figure. No Caption Available.

Use of CFM

The CFM may detect cerebral ischaemia; burst suppression (periods of increasingly prolonged electrical silence) provide an early warning.

Sedation produces a fall in baseline to <5μV, equivalent to burst suppression. This is equivalent to maximum reduction in cerebral VO_2 and no further benefit would be gained from additional sedation.

Seizure activity may be detected in patients despite apparently adequate clinical control or where muscle relaxants have been used.

Typical CFM patterns
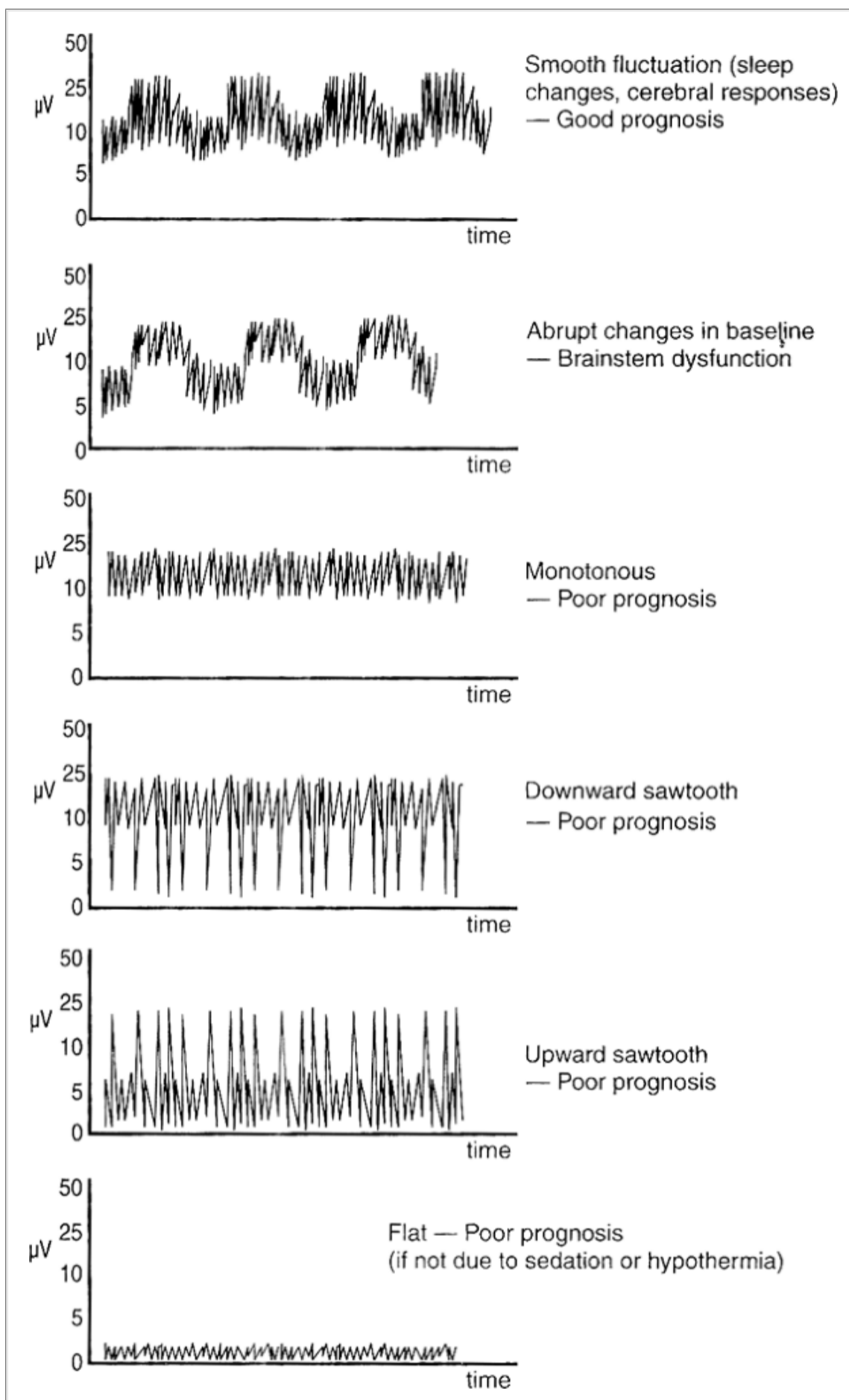
Figure. No Caption Available.

Other neurological monitoring

Cerebral blood flow (CBF)

CBF can be measured by radioisotopic techniques utilising tracers such as xenon-133 given intravenously or by inhalation. This remains a research tool in view of the radioactivity exposure and the usual need to move the patient to a gamma-camera. However, portable monitors are now available. Middle cerebral artery (MCA) blood flow can be determined non-invasively by transcranial Doppler ultrasonography. The pulsatility index (PI) relates to cerebrovascular resistance with a rise in PI indicating a rise in resistance and cerebral vasospasm.

Vasospasm can also be designated when the MCA blood flow velocity exceeds 120cm/s and severe vasospasm when velocities >200cm/s. Low values of common carotid end-diastolic blood flow and velocity have been shown to be highly discriminating predictors of brain death. Impaired reactivity of CBF to changes in PCO_2 (in normals 3–5% per mmHg PCO_2 change) is another marker of poor outcome.

Near-infra red spectroscopy (NIRS)

- Near-infrared (700–1000nm) light propagated across the head is absorbed by haemoglobin (oxy- and de-oxy), myoglobin and oxidised cytochrome aa_3 (the terminal part of the respiratory chain involved in oxidative

phosphorylation).

- The sum of (oxy- + deoxy-) haemoglobin is considered an index of cerebral blood volume (CBV) change, and the difference as an index of change in haemoglobin saturation assuming no variation occurs in CBV. CBV and flow can be quantified by changing the FIO_2 and measuring the response.

- Cerebral blood flow is measured by a modification of the Fick principle. Oxyhaemoglobin is the intravascular non-diffusible tracer, its accumulation being proportional to the arterial inflow of tracer. Good correlations have been found with the xenon-133 technique.

- Cytochrome aa_3 cannot be quantified by NIRS but its redox status may be followed to provide some indication of mitochondrial function.

- Movement artefact must be avoided and some devices require reduction of ambient lighting.

Lactate

The brain normally utilises lactate as a fuel; however, in states of severely impaired cerebral perfusion the brain may become a net lactate producer with the venous lactate rising above the arterial value. A lactate oxygen index can be derived by dividing the venous–arterial lactate difference by the arterio-jugular venous oxygen difference. Values >0.08 are consistently seen with cerebral ischaemia.

See also:

Laboratory Monitoring

Urea and creatinine

Measured in blood, urine and, occasionally, in other fluids such as abdominal drain fluid (e.g. ureteric disruption, fistulae)

Urea

A product of the urea cycle resulting from ammonia breakdown, it depends upon adequate liver function for its synthesis and adequate renal function for its excretion. Low levels are thus seen in cirrhosis and high levels in renal failure. Uraemia is a clinical syndrome including lethargy, drowsiness, confusion, pruritus and pericarditis resulting from high plasma levels of urea (or, more correctly, nitrogenous waste products—azotaemia).

The ratio of urine:plasma urea may be useful in distinguishing oliguria of renal or pre-renal origins. Higher ratios (>10:1) are seen in pre-renal conditions, e.g. hypovolaemia, whereas low levels (<4:1) occur with direct renal causes.

24-h measurement of urinary urea (or nitrogen) excretion has been previously used as a guide to nutritional protein replacement but is currently not considered a useful routine tool.

Creatinine

A product of creatine breakdown, it is predominantly derived from skeletal muscle and is also renally excreted. Low levels are found with malnutrition and high levels with muscle breakdown (rhabdomyolysis) and impaired excretion (renal failure). In the latter case, a creatinine value >120 µmol/l suggests a creatinine clearance <25ml/min.

The usual ratio for plasma urea (mmol/l) to creatinine (µmol/l) is approximately 1:10. A much lower ratio in a critically ill patient is suggestive of rhabdomyolysis whereas higher ratios are seen in cirrhosis, malnutrition, hypovolaemia and hepatic failure.

The ratio of urine:plasma creatinine may help distinguish between oliguria of renal or pre-renal origins. Higher ratios (>40) are seen in pre-renal conditions and low levels (<20) with direct renal causes.

Creatinine clearance is a measure of glomerular filtration. Once filtered, only small amounts of creatinine are reabsorbed. Normally it exceeds 100ml/min.

Normal plasma ranges

Urea	2.5–6.5mmol/l
Creatinine	70–120µmol/l (depends on lean body mass)

See also:

Electrolytes (Na^+, K^+, Cl^-, HCO_3^-)

Measured accurately by direct-reading ion-specific electrodes from plasma or urine, though are sensitive to interference by excess liquid heparin.

Sodium, potassium

Plasma levels may be elevated but poorly reflect intracellular (approximately 3–5mmol/l for Na^+, 140–150mmol/l for K^+) or total body levels. Plasma potassium levels are affected by plasma H^+ levels; a metabolic acidosis reduces urinary potassium excretion while an alkalosis will increase excretion.

Older measuring devices such as flame photometry or indirect-reading ion-specific electrodes gave spuriously low plasma Na^+ levels with concurrent hyperproteinaemia or hypertriglyceridaemia.

Urinary excretion depends on intake, total body balance, acid–base balance, hormones (including anti–diuretic hormone, aldosterone, corticosteroids, atrial natriuretic peptide), drugs (particularly diuretics, non-steroidal anti-inflammatories and ACE inhibitors), and renal function.

In oliguria, a urinary Na^+ level <10mmol/l suggests a pre-renal cause whereas >20mmol/l is seen with direct renal damage. This does not apply if diuretics have been given previously.

Chloride, bicarbonate

Bicarbonate levels vary with acid–base balance.

In the kidney, Cl^- reabsorption is increased when HCO_3^- reabsorption is decreased, and vice versa. Plasma $[Cl^-]$ thus tends to vary inversely with plasma $[HCO_3^-]$, keeping the total anion concentration normal. A raised $[Cl^-]$ (producing a hyperchloraemic metabolic acidosis) may be seen with administration of large volumes of isotonic saline or isotonic saline-containing colloid solutions. Hyperchloraemia is also found with experimental salt water drowning but rarely seen in actual cases.

Anion gap

The anion gap is the difference between unestimated anions (e.g. phosphate, ketones, lactate) and cations.

In metabolic acidosis an increased anion gap occurs with renal failure, ingestion of acid, ketoacidosis and hyperlactataemia, whereas a normal anion gap (usually associated with hyperchloraemia) is found with decreased acid excretion (e.g. Addison's disease, renal tubular acidosis) and loss of base (e.g. diarrhoea, pancreatic/biliary fistula, acetazolamide, ureterosigmoidostomy).

Normal plasma ranges

Sodium	135–145mmol/l
Potassium	3.5–5.3mmol/l
Chloride	95–105mmol/l
Bicarbonate	23–28mmol/l
Anion gap = plasma $[Na^+]$ + $[K^+]$ - $[HCO3^-]$ - $[Cl^-]$	

Normal range	8–16mmol

See also:

Haemo(dia)filtration (1), p62; Haemo(dia)filtration (2), p64; Peritoneal dialysis, p66; Nutrition—use and indications, p78; Urinalysis, p166; Crystalloids, p176; Diuretics, p212; Tachyarrhythmias, p316; Bradyarrhythmias, p318; Acute renal failure—diagnosis, p332; Acute renal failure—management, p334; Vomiting/gastric stasis, p338; Diarrhoea, p340; Acute liver failure, p360; Hypernatraemia, p416; Hyponatraemia, p418; Hyperkalaemia, p420; Hypokalaemia, p422; Metabolic acidosis, p434; Metabolic alkalosis, p436; Diabetic ketoacidosis, p442; Hyperosmolar diabetic emergencies, p444; Hypoadrenal crisis, p448; Poisoning—general principles, p452; Rhabdomyolysis, p528

Calcium, magnesium and phosphate

Calcium

Plasma calcium levels have been traditionally corrected to plasma albumin levels; this is now considered irrelevant, particularly at the low albumin levels seen in critically ill patients. Measurement of the ionised fraction is now considered more pertinent since it is the ionised fraction that is responsible for the extracellular actions of calcium, with changes in the ionised fraction being responsible for the symptomatology.

High calcium levels occur with hyperparathyroidism, certain malignancies and sarcoidosis while low levels are seen in renal failure, severe pancreatitis and hypoparathyroidism.

Magnesium

Plasma levels poorly reflect intracellular or whole body stores, 65% of which is in bone and 35% in cells. The ionised fraction is approximately 50% of the total level.

High magnesium levels are seen with renal failure and excessive administration; this rarely requires treatment unless serious cardiac conduction problems or neurological complications (respiratory paralysis, coma) intervene.

Low levels occur following severe diarrhoea, diuretic therapy, alcohol abuse, and accompany hypocalcaemia.

Magnesium is used therapeutically for a number of conditions including ventricular and supraventricular arrhythmias, eclampsia, seizures, asthma and after myocardial infarction. Supranormal plasma levels of 1.5–2.0mmol/l are often sought.

Phosphate

High levels are seen with renal failure and in the presence of an ischaemic bowel. Low levels (sometimes <0.1mmol/l) occur with critical illness, chronic alcoholism and diuretic usage and may possibly result in muscle weakness, failure to wean and myocardial dysfunction.

Normal plasma ranges

Calcium	2.2–2.6mmol/l
Ionised calcium	1.05–1.2mmol/l
Magnesium	0.7–1.0mmol/l
Phosphate	0.7–1.4mmol/l

See also:

IPPV—assessment of weaning, p18; Plasma exchange, p68; Nutrition—use and indications, p78; Tachyarrhythmias, p316; Pancreatitis, p354; Generalised seizures, p372; Hypomagnesaemia, p424; Hypercalcaemia, p426; Hypocalcaemia, p428; Hypophosphataemia, p430; Pre-eclampsia and eclampsia, p538

Cardiac function tests

The importance of biochemical markers of myocardial necrosis has been emphasised by a consensus document from the European Society of Cardiology and American College of Cardiology. The diagnosis of myocardial infarction was redefined as a typical rise and fall in troponin, or a more rapid rise and fall in CK-MB, with at least one of the following:

- Ischaemic symptoms

- Development of pathological Q waves on ECG

- ECG ST elevation or depression

- Coronary intervention

Troponins

Troponins are bound to the actin filament within muscles and are involved in excitation–contraction coupling. Both cardiac troponin T and troponin I are coded by specific genes and are immunologically distinct from those in skeletal muscle. Neither is detectable in normal healthy individuals but both are released into the bloodstream from cardiomyocytes damaged by necrosis, toxins and inflammation. They become detectable by 4–6h after myocardial injury, peak at 14–18h, and persist for up to 12 days. Current assays are highly specific as they use recombinant human cardiac tropinin T as a standard.

Due to their high sensitivity, plasma levels rise with other cardiac insults, e.g. tachycardia (SVT/VT), pericarditis, myocarditis, sepsis, heart failure, severe exertion and pulmonary embolism. The degree of rise post-MI or during critical illness correlates with a worse outcome.

A positive test is when the cardiac troponin T or I value exceeds the 99th percentile of values for a control group on ≥1 occasion during the first 24h after the index clinical event. For cardiac troponin T this is quoted as 0.05–0.1ng/ml though many labs now consider values >0.03ng/ml as positive. Values for cardiac troponin I depend on the particular assay used (usually >0.5–1.5ng/ml). The negative predictive value after an acute MI is probably strongest after 6h. Sensitivity peaks at 12h but at the expense of a lower specificity. With renal dysfunction, higher levels are needed to diagnose myocardial damage due to impaired excretion.

Cardiac enzymes

Creatine kinase (CK) is detectable in plasma within a few hours of myocardial injury. The cardiac-specific isoform (CK-MB) can be measured if there is concurrent skeletal muscle injury. CK and aspartate aminotransferase (AST) peak by 24h and fall over 2–3 days whereas the rise and subsequent fall in plasma lactate dehydrogenase takes 1–2 days longer.

Brain (or B-type) natriuretic peptide (BNP)

Cardiomyocytes produce and secrete cardiac natriuretic peptides. Plasma levels rise in a variety of conditions but high levels are predominantly associated with heart failure, and increase in relation to severity. A sensitivity of 90–100% is claimed, whereas specificity is approximately 70–80%. Numerous commercial assays for B-type natriuretic peptide (BNP) or proBNP are now available, each with their own diagnostic range. They are useful as a screening tool for patients presenting with dyspnoea, for prognostication, and for titration of therapy. Levels rise in the elderly, in renal failure, and in pulmonary diseases causing right ventricular overload (e.g. pulmonary embolus).

Figure. No Caption Available.
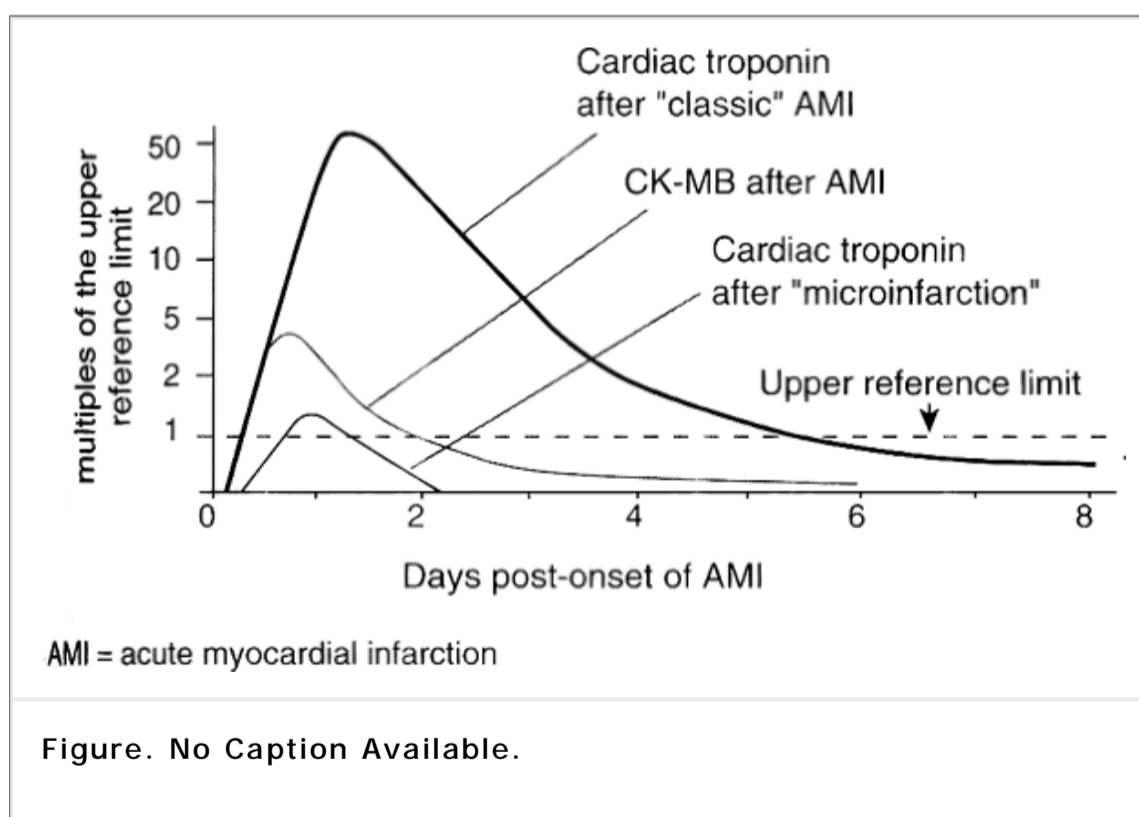
Key paper

Antman E et al. Myocardial infarction redefined—a consensus document of The Joint European Society of Cardiology/American College of Cardiology committee for the redefinition of myocardial infarction. J Am Coll Cardiol 2000; 36:959–69

McCullough PA, et al. B-type natriuretic peptide and clinical judgment in emergency diagnosis of heart failure: analysis from Breathing Not Properly (BNP) Multinational Study. Circulation 2002; 106:416–22

See also:

Liver function tests

Hepatic metabolism proceeds via Phase I enzymes (oxidation and phosphorylation) and then subsequently to Phase II enzymes (glucuronidation, sulphation, acetylation). Phase I enzyme reactions involve cytochrome P450.

Markers of hepatic damage

- Alanine aminotransferase (ALT)
- Aspartate aminotransferase (AST)
- Lactate dehydrogenase (LDH)

Patterns and ratios of various enzymes are variable and unreliable diagnostic indicators. Measurement of ALT alone is usually sufficient. It is more liver-specific but less sensitive than AST and has a longer half-life.

AST is not liver-specific but is a sensitive indicator of hepatic damage. The plasma level is proportional to the degree of hepatocellular damage. Low levels occur in extrahepatic obstruction and inactive cirrhosis.

LDH is insensitive and non-specific. Isoenzyme electrophoresis is needed to distinguish cardiac, erythrocyte, skeletal muscle and liver injury.

Acute phase reactants such as C-reactive protein (CRP) are also produced by the liver. Levels increase during critical illness and following hepatocellular injury.

Markers of cholestasis

- Bilirubin
- Alkaline phosphatase
- Gamma-glutamyl transferase (γ-GT)

Bilirubin is derived from Hb released from erythrocyte breakdown and conjugated with glucuronide by the hepatocytes. The conjugated fraction is water-soluble whereas the unconjugated fraction is lipid-soluble. Levels are increased with intra- and extrahepatic biliary obstruction (predominantly conjugated), hepatocellular damage and haemolysis (usually mixed picture). Jaundice is detected when levels >45µmol/l.

Alkaline phosphatase is released from bone, liver, intestine and placenta. In the absence of bone disease (check Ca^{2+} and PO_4^{3-}) and pregnancy, raised levels usually indicate biliary tract dysfunction.

A raised γ-GT is a highly sensitive marker of hepatobiliary disease. Increased synthesis is induced by obstructive cholestasis, alcohol, various drugs and toxins, acute and chronic hepatic inflammation.

Markers of reduced synthetic function

- Albumin
- Clotting factors
- Cholinesterase

Albumin levels fall during critical illness due to protein catabolism, capillary leak, decreased synthesis, dilution with artificial colloids.

Coagulation factors II, VII, IX and X are liver-synthesised. Over 33% of functional hepatic mass must be lost before any abnormality is seen.

Indicators of function

- Lidocaine metabolites (MegX)

Indicators of hepatic blood flow

- Indocyanine green clearance
- Bromosulphthalein clearance

Normal plasma ranges

Albumin	35–53g/l
Bilirubin	3–17µmol/l
Conjugated bilirubin	0–6µmol/l
Alanine aminotransferase	5–50U/l
Alkaline phosphatase	100–280U/l
Aspartate aminotransferase	11–55U/l
Cholinesterase	2.3–9.0KU/l
γ-glutamyl-transferase	5–37U/l
Lactate dehydrogenase	230–460U/l

See also:

Full blood count

Haemoglobin

A raised haemoglobin occurs in polycythaemia (primary and secondary to chronic hypoxaemia) and in haemoconcentration. Anaemia may be due to reduced red cell mass (decreased red cell production or survival) or haemodilution. The latter is common in critically ill patients. In severe anaemia there may be a hyperdynamic circulation which, if severe, may decompensate to cardiac failure. In this case, blood transfusion must be performed with extreme care to avoid fluid overload, or in association with plasmapheresis. Differential diagnosis of anaemia includes:

Reduced MCV

Iron deficiency (anisocytosis and poikilocytosis)

Raised MCV

Vitamin B_{12} or folate deficiency

Alcohol excess

Liver disease

Hypothyroidism

Normal MCV

Anaemia of chronic disease

Bone marrow failure (e.g. acute folate deficiency)

Hypothyroidism

Haemolysis (increased reticulocytes and bilirubin)

White blood cells

A raised white cell count is extremely common in critical illness. Causes of changes in the differential count include:

Neutrophilia	Lymphocytosis	Eosinophilia
Bacterial infection	Brucellosis	Asthma
Trauma and surgery	Typhoid	Allergic conditions
Burns	Myasthenia gravis	Parasitaemia
Haemorrhage	Hyperthyroidism	
Inflammation	Leukaemia	
Steroid therapy		
Leukaemia		
Neutropenia	**Lymphopenia**	
Viral infections	Steroid therapy	
Brucellosis	SLE	
Typhoid	Legionnaire's disease	
Tuberculosis	AIDS	
Sulphonamide treatment		
Severe sepsis		
Hypersplenism		
Bone marrow failure		

Barrier nursing may be used for neutropenia $<1.0 \times 10^9$/l.

Platelets

Correct interpretation of platelet counts requires blood to be taken by a venepuncture. Arterial blood is commonly taken from an indwelling cannula but is not ideal. Thrombocytopenia is due to decreased platelet production (bone marrow failure, vitamin B_{12} or folate deficiency), decreased platelet survival (ITP, TTP, infection, hypersplenism, heparin therapy), increased platelet consumption (haemorrhage, DIC) or *in vivo* aggregation giving an apparent thrombocytopenia; this should be checked on a blood film. Spontaneous bleeding is associated with platelet counts $<20 \times 10^9$/l and platelet cover is required for procedures or traumatic bleeds at counts $<50 \times 10^9$/l.

Normal ranges

Haemoglobin	13–17g/dl (men), 12–16g/dl (women)
MCV	76–96fl
White cell count	4–11 ×10^9/l
Neutrophils	2–7.5 ×10^9/l
Lymphocytes	1.3–3.5 ×10^9/l
Eosinophils	0.04–0.44 ×10^9/l
Basophils	0–0.1 ×10^9/l
Monocytes	0.2–0.8 ×10^9/l
Platelets	150–400 ×10^9/l

See also:

Coagulation monitoring

Basic coagulation screen

The basic screen consists of a platelet count, prothrombin time, activated partial thromboplastin time and thrombin time. Close attention to blood sampling technique is very important for correct interpretation of coagulation tests. Drawing blood from indwelling catheters should, ideally, be avoided since samples may be diluted or contaminated with heparin. The correct volume of blood must be placed in the sample tube to avoid dilution errors. Laboratory coagulation tests are usually performed on citrated plasma samples taken into glass tubes.

Specific coagulation tests

Activated clotting time (ACT)

Sample tube contains celite, a diatomaceous earth, which activates the contact system; thus the ACT predominantly tests the intrinsic pathway. The ACT is prolonged by heparin therapy, thrombocytopenia, hypothermia, haemodilution, fibrinolysis and high dose aprotinin. Normal is 100–140s.

Thrombin time (TT)

Sample tube contains lyophilised thrombin and calcium. Thrombin bypasses the intrinsic and extrinsic pathways such that the coagulation time tests the common pathway with conversion of fibrinogen to fibrin. The TT is prolonged by fibrinogen depletion, e.g. fibrinolysis or thrombolysis, and heparin via antithrombin III dependent interaction with thrombin. A high dose TT is more sensitive to heparin anticoagulation than fibrinogen levels. Normal range is 12–16s.

Prothrombin time (PT)

Sample tube contains tissue factor and calcium. Tissue factor activates the extrinsic pathway. The PT is prolonged with coumarin anticoagulants, liver disease and vitamin K deficiency. Normal range is 12–16s. The International Normalised Ratio (INR) relates PT to control and is normally 1.

Activated partial thromboplastin time (APTT)

Sample tube contains kaolin and cephalin as a platelet substitute to activate the intrinsic pathway. The APTT is prolonged by heparin therapy, DIC, severe fibrinolysis, von Willebrand factor, factor VIII, factor X1 or factor XIII deficiencies. Normal range is 30–40s.

D-dimers and fibrin degradation products (FDPs)

Fibrin fragments are released by plasmin lysis. FDPs can be assayed by an immunological method; they are often measured in the critically ill to confirm disseminated intravascular coagulation. A level of 20–40µg/ml is common

post-operatively, in sepsis, trauma, renal failure and DVT. Raised levels do not distinguish fibrinogenolysis and fibrinolysis. Assay of the d-dimer fragment is more specific for fibrinolysis, e.g. in DIC, since it is only released after fibrin is formed.

Coagulation factor assays

Assays are available for all coagulation factors and may be used for diagnosis of specific defects. As heparins inhibit factor Xa activity, the factor Xa assay is therefore the most specific method of controlling low molecular weight heparin therapy. Since this assay is not dependent on contact system activation, it also avoids the effects of aprotinin when monitoring heparin therapy.

The coagulation cascade – new concept

Figure. No Caption Available.

The traditional coagulation cascade consisting of extrinsic, intrinsic and common pathways is now considered outmoded, inconsistent with clinical observations, and inadequate to explain the pathways leading to haemostasis *in vivo*. This schema has been replaced recently by a cell-based model with the major initiating haemostasis event *in vivo* being the action of factor VIIa and tissue factor (TF) at the site of injury.

See also:

Bacteriology

Microbiology samples should, if possible, be taken prior to commencement of antimicrobial therapy. In severe infections, broad spectrum antimicrobials should be started without awaiting results. Sampling sites include those suspected clinically of harbouring infection or, if a specific site cannot be identified clinically, blood, urine and sputum samples. In severe infection, indwelling intravascular catheters should be replaced and the catheter tips sent for culture. Samples should be sent to the laboratory promptly to allow early incubation and to prevent potentially misleading growth. Swabs must be sent in the appropriate transport media.

Blood cultures

In order to avoid skin contamination, the skin should be cleaned with alcohol and allowed to dry thoroughly before venepuncture. A 5–20ml blood sample is withdrawn and divided into anaerobic and aerobic culture bottles. In addition, cultures should be taken through indwelling intravascular catheters if catheter-related sepsis is suspected. All samples must be clearly labelled. Culture bottles are incubated and examined frequently for bacterial growth. Positive cultures must be interpreted in light of the clinical picture; an early pure growth from multiple bottles is likely to be significant, although cultures from critically ill patients may appear later or not at all due to antibiotic therapy. Any Gram negative isolates or *Staph. aureus* are usually taken as significant.

Urine

Catheter specimens are usually obtained from the critically ill. The sampling site should be prepared aseptically prior to sampling. The specimen should be sent to the laboratory immediately and examined microscopically for organisms, casts and crystals. Urine is plated onto culture medium with a calibrated loop and incubated for 18–24h prior to examination. Bacteria $>10^8$/l (or a pure growth of 10^5/l) represent a significant growth. All catheter specimens show bacterial growth if the catheter has been in place for >2days. Isolation of the same organism from blood confirms a significant culture.

Sputum

Sputum samples are easily contaminated during collection, particularly specimens from non-intubated patients. Suction specimens from intubated patients can be taken via a sterile suction catheter, protected catheter brush or from specific lung segments via a bronchoscope. Gram negative bacteria are frequently isolated from tracheal aspirates of intubated patients; only deep suction specimens are significant. Blood cultures should accompany sputum specimens in the diagnosis of pneumonia. Samples should be sent to the laboratory immediately.

Pus samples and wound swabs

Aspirated pus must be sent to the laboratory immediately or a swab sample may be taken and sent in transport medium. Pus is preferable for bacterial isolation.

Typical ICU-acquired nosocomial infections

Pneumonia due to *Pseudomonas aeruginosa, Staph. aureus, Klebsiella* spp., *Enterobacter* spp.

Urinary infection with *E. coli, Ps. aeruginosa, Klebsiella* spp., Proteus spp.

Catheter related sepsis—*Staph. aureus*, coagulase negative staphylococci

See also:

Virology, serology and assays

Antibiotic assays

Antibiotic assays are usually performed for drugs with a narrow therapeutic range, such as aminoglycosides and vancomycin. It is not usual to request an assay on day 1 of treatment. Thereafter, samples are taken daily prior to giving a dose and at 1h after an intravenous injection or infusion.

Serology

A clotted blood specimen allows antibodies to viral and atypical antigens to be assayed. It is usual to send acute and convalescent (14 days) serum to determine rising antibody titres. Single sample titres may be used to determine previous exposure and carrier status.

Hepatitis B

Serology includes hepatitis B surface antigen as a screening test and hepatitis B core antigen to determine infectivity. There is a 10% carrier rate in South East Asians. Serology should be sent in all high risk patients, e.g. jaundice, IV drug abuse, homosexuals, prostitutes, those with tattoos or unexplained hepatic enzyme abnormalities. In addition, hepatitis B status should be known in staff who suffer accidental exposure to body fluids, e.g. through needlestick injury. Those who are not immune may be treated with immunoglobulin.

HIV

Since HIV positive status carries consequences for lifestyle and insurance, it should rarely be assessed without prior counselling and consent. The CD4 count may be used to assess the likelihood of symtomatology being AIDS-related, although this will fall further with acute critical illness; again, consent should usually be sought pre-testing. High risk patients should be considered for testing, e.g. homosexual males, intravenous drug abusers, haemophiliacs, Central African origin. In critically ill patients such consent can rarely be obtained and unconsented testing may be used where management may change significantly with knowledge of the HIV status, or where organ donation is being considered. Most AIDS-related infections can be adequately treated without knowledge of the HIV status. Patients or staff who are recipients of a needlestick injury can be treated with antiretroviral therapies if risk is high.

Viral culture

Most commonly used for CMV. Samples of blood, urine or bronchial aspirate may be sent for DEAFF (detection of early antigen fluorescent foci). Herpes virus infections may be detected by electron microscopy of samples (including pustule fluid) and adenovirus in immunosuppressed patients with a chest infection.

Fungi

Candida and *Aspergillus* can be assessed by culture ± antigen tests. *Cryptococcus* can be detected by Indian ink stain in biopsy samples.

Other tests

Other tests available to make microbiological diagnoses include antigen testing for certain bacteria (e.g. pneumococcus), and PCR (polymerase chain reaction) which amplifies the microbial DNA. PCR is an extremely sensitive test for specific organisms. However, it is prone to environmental contamination (e.g. from airborne spores) and it cannot distinguish between colonisation and infection.

Common serology for critically ill patients

Hepatitis A

Hepatitis B

Hepatitis C

HIV

CMV

Mycoplasma pneumoniae

Legionella pneumophila

Antibiotic therapeutic levels

	Trough (mg/l)	Peak (mg/l)
Amikacin	<8	30
Gentamicin	<2	4–10*
Tobramycin	<2	4–10
Vancomycin	<8	20–30
*Seek microbiological advice if once daily gentamicin is used		

See also:

Bacteriology, p158; Urinalysis, p166; Antimicrobials, p260; Acute chest infection (1), p288; Acute chest infection (2), p290; Jaundice, p358; Acute liver failure, p360; Tetanus, p390; Botulism, p392; HIV related disease, p488; Pyrexia (1), p518; Pyrexia (2), p520

Toxicology

Purpose

Samples taken from blood, urine, vomitus or gastric lavage (depending on drug or poison ingested) for:

- Monitoring of therapeutic drug levels (usually plasma) and avoidance of toxicity, e.g. digoxin, aminoglycosides, lithium, phenytoin

- Identification of unknown toxic substances (e.g. cyanide, amphetamines, opiates) causing symptomatology and/or pathology. Always take a urine sample for analysis.

- Confirmation of toxic plasma levels and monitoring of treatment effect, e.g. paracetamol, aspirin

- Medicolegal, e.g. alcohol, recreational drugs following road trauma

Samples

Confirm with chemistry laboratory ± local poisons unit as to which, how, and when body fluid samples should be taken for analysis, e.g. peak/trough levels for aminoglycosides, urine samples for out-of-hospital poisoning, repeat paracetamol levels to monitor efficacy of treatment

See also:

Virology, serology and assays, p160; Poisoning—general principles, p45

Miscellaneous Monitoring

Urinalysis

Techniques

- Biochemical/metabolic:
    - i. colorimetric 'dipsticks' read manually from reference chart or by automated machine within 15s—2min of dipping in urine (see manufacturer's instructions). Usually performed at the bedside.
    - ii. sodium and potassium levels can be measured in most analysers used for plasma electrolyte measurement. Recalibration of the machine or special dilution techniques may be required.
    - iii. laboratory analysis
- Haematological—either by dipstick or laboratory testing
- Microbiological—microscopy, culture, sensitivity; antigen tests
- Renal disease—usually by microscopy + laboratory testing

Associated tests

Some of the above investigations are performed in conjunction with a blood test, e.g. urine:plasma ratios of urea, creatinine and osmolality to distinguish renal from pre-renal causes of oliguria, 24h urine collection plus plasma creatinine for creatinine clearance estimation.

Cautions

- White blood cells, proteinuria and mixed bacterial growths are routine findings in catheterised patients and do not necessarily indicate infection.
- A 'positive' dipstick test for blood does not differentiate between haematuria, haemoglobinuria or myoglobinuria.
- Only conjugated bilirubin is excreted into the urine.
- Urinary sodium and potassium levels are increased by diuretic usage.

Urinalysis tests

Biochemical/metabolic:	
pH	dipstick
glucose	dipstick
ketones	dipstick
protein	dipstick, laboratory
bilirubin	dipstick
sodium, potassium	electrolyte analyser, laboratory
urea, creatinine, nitrogen	laboratory
osmolality	laboratory
specific gravity	bedside gravimeter, laboratory
myoglobin	laboratory, positive dipstick to blood
drugs, poisons	sent to Poisons Reference Laboratory
Haematological:	
red blood cells	microscopy, positive dipstick to blood
haemoglobin	laboratory, positive dipstick to blood
neutrophils	dipstick, laboratory
Microbiological:	
bacteriuria	microscopy, culture
TB	microscopy, culture (early morning specimens)
Legionnaire's disease	laboratory
Nephro-urological:	
haematuria	microscopy
granular casts	microscopy
protein	laboratory
sodium, potassium	electrolyte analyser, laboratory
malignant cells	cytology

See also:

Indirect calorimetry

Calorimetry refers to the measurement of energy production. Direct calorimetry is the measurement of heat production in a sealed chamber but is impractical for critically ill patients. Indirect calorimetry measures the rate of oxidation of metabolic fuels by detecting the volume of O_2 consumed and CO_2 produced. The ratio of CO_2 production to O_2 utilisation (respiratory quotient or RQ) defines which fuels are being utilised (see table). Knowledge of the oxygen utilisation by the various fuels allows the calculation of energy production. Carbohydrate and fat are oxidised to CO2 and water producing 15–17 and 38–39kJ/g respectively. Protein is oxidised to CO2, water and nitrogen (subsequently excreted as urea) producing 15–17kJ/g.

Technique of indirect calorimetry

Inspiratory and mixed expiratory gases must be sampled. O_2 concentration may be measured by a fuel cell sensor or a fast response, paramagnetic sensor. CO_2 is usually measured by infrared absorption. Sensors may be calibrated with reference to known concentrations of standard gas or by burning a pure fuel with a predictable O_2 consumption. Measurements are usually made at ambient temperature, pressure and humidity prior to conversion to standard temperature, pressure and humidity. In order to calculate metabolic rate (energy expenditure) inspired and expired minute volumes are required. It is common for one minute volume to be measured and the other derived from a Haldane transformation:

$$V_I = V_E \times \frac{N_E}{N_I}$$

The nitrogen concentrations are assumed to be the concentration of gas which is not O_2 or CO_2. Calculation of energy expenditure utilises a modification of the de Weir formula Energy expenditure = $(3.94\ VO_2 + 1.11\ VCO_2) \times 1.44$

Although it is possible to calculate the rate of protein metabolism by reference to the urinary urea concentration, and therefore to separate non-protein from protein energy expenditure, the resulting modification of the above formula is not usually clinically significant.

Errors associated with indirect calorimetry

Underestimate VCO_2	H^+ ion loss, haemodialysis, haemofiltration
Overestimate VCO_2	hyperventilation, $HCO3^-$ infusion
Underestimate VO_2	free radical production, unmeasured O_2 supply
$FIO_2 > 0.6$	small difference between inspired and expired O_2
Loss of volume	circuit leaks, bronchopleural fistula

Use of indirect calorimetry

Helps to match nutritional intake to energy expenditure. It is important to feed critically ill patients appropriately, avoiding both underfeeding and overfeeding (see table). Indirect calorimetry may also be used to assess the work of breathing by assessing the change in VO_2 during weaning from mechanical ventilation. The VO_2 change may also be used to assess appropriate levels of sedation and analgesia.

Respiratory quotients for various metabolic fuels

Ketones	0.63
Fat	0.71
Protein	0.80
Carbohydrate	1.00

The whole body RQ depends on the fuel or combination of fuels being utilised. Normally a combination of fat and carbohydrate are utilised with a RQ of 0.8.

Lipogenesis associated with both sepsis and overfeeding may give a RQ of 1.1–1.3

See also:

IPPV—assessment of weaning, p18; Nutrition—use and indications, p78; Enteral nutrition, p80; Parenteral nutrition,

Lactate

Measurement of blood lactate

Analysers are available to allow rapid measurement of blood or plasma lactate on small samples, using enzyme-based methods. The enzymatic conversion of lactate to pyruvate is an oxygen utilising reaction. The extraction of oxygen from the sample can be detected by a sensitive oxygen fuel cell sensor and is directly proportional to the sample lactate concentration. A whole blood sample (venous or arterial since there is no practical difference) is collected into a heparin fluoride tube to prevent coagulation and glycolysis (lactate producing). Nitrite may be used in the sample tube to convert haemoglobin to the met form, thus avoiding uptake of oxygen during the enzyme reaction. The enzymatic method is specific for the L-isomer and will not, therefore, detect D-lactate (e.g. in short bowel syndrome). Normal arterial whole blood lactate concentration is <1.5mmol/l. Lactate may also be measured from regional sites as an aid to the assessment of regional perfusion (e.g. arterial–jugular bulb difference).

Biochemistry of lactate production

Pyruvate is the end product of glycolysis. Most is then metabolised by pyruvate dehydrogenase to acetyl CoA, the major substrate for the Krebs cycle. However, in conditions of mitochondrial dysfunction (e.g. cellular hypoxia, sepsis) more pyruvate is converted to lactate by lactate dehydrogenase.

Lactate is a buffer not an acid so a high blood lactate is not, therefore, synonymous with lactic acidosis. In continuous haemofiltration the replacement fluid is usually buffered with lactate at 35–45mmol/l; thus blood lactate levels will rise without acidosis.

Causes of lactic acidosis

Lactic acidosis occurs when production of lactic acid is in excess of removal. The major sources are skeletal muscle, brain and red blood cells. Removal is mainly by metabolism to glucose in the liver and kidney. Hepatic removal is impaired by poor perfusion and acidosis. Lactic acidosis is traditionally classified as type A or type B. Type A refers to excess production when tissue oxygenation is inadequate. Type B occurs where there is no systemic tissue hypoxia. Epinephrine therapy may cause accelerated aerobic glycolysis and pyruvate production in excess of mitochondrial needs; this may produce an increasing metabolic acidosis often out of proportion to the patient's clinical status. In sepsis, hyperlact ataemia is mainly due to increased muscle Na^+K^+-ATPase activity. Treatment of metabolic acidosis with sodium bicarbonate solution may increase lactate production. A severe and persistent type A lactic acidosis is associated with a poor outcome.

Identifying type A lactic acidosis

Evidence of poor tissue perfusion may be obvious clinically. Calculation of arterial DO_2 may confirm inadequate tissue oxygen delivery but a normal DO_2 does not guarantee adequacy of supply.

Key trial

Totaro RJ, Raper RF. Epinephrine-induced lactic acidosis following cardiopulmonary bypass. Crit Care Med 1997; 25:1693–9

See also:

Colloid osmotic pressure

Colloid osmotic pressure (COP) is the pressure required to prevent net fluid movement between two solutions separated by a selectively permeable membrane when one contains a greater colloid concentration than the other. The selectively permeable membrane should impede the passage of colloid molecules but not small ions and water. COP is determined by number of molecules rather than type. However, most solutions exhibit non-ideal behaviour due to intermolecular interactions and electrostatic effects. Hence COP cannot be inferred from plasma protein concentrations; it must be measured.

Measurement of COP

In a membrane oncometer the plasma sample is separated from a reference 0.9% saline solution by a membrane with a molecular weight exclusion between 10,000 and 30,000Da. The reference solution is in a closed chamber containing a pressure transducer. Saline will pass to the sample chamber by colloid osmosis creating a negative pressure in the reference chamber. When the negative pressure prevents any further flow across the membrane, it is equal to the COP of the sample. Normal plasma COP is 25–30mmHg.

Clinical use of COP measurement

Assessing significance of reduced plasma proteins

Plasma albumin levels are almost invariably reduced in critically ill patients. Causes include interstitial leakage, failed synthesis and increased metabolism. However, the same group of patients often have raised levels of acute phase proteins which contribute to COP. Since there is no evidence that correction of plasma albumin levels is beneficial, many clinicians correct plasma volume deficit with artificial colloid. These will contribute to COP while also reducing hepatic albumin synthesis. If COP is maintained >20mmHg it is likely that reduced plasma albumin levels are of no significance.

Avoiding pulmonary oedema

It has been suggested that a difference between COP and pulmonary artery wedge pressure >6mmHg minimises the risk of pulmonary oedema. However, in the face of severe capillary leak it is unlikely that pulmonary oedema can be avoided if plasma volumes are to be maintained compatible with circulatory adequacy. Conversely, a normal COP would not necessarily prevent pulmonary oedema in severe capillary leak; the contribution of COP to fluid dynamics in this situation is much reduced.

Selection of appropriate fluid therapy

It is difficult not to support the use of colloid fluids in hypo-oncotic patients. In patients with renal failure the repeated use of colloid fluid may lead to a hyperoncotic state. This is associated with tissue dehydration and failure of glomerular filtration (thus prolonging the renal failure). Measurement of a high COP in patients who have been treated with artificial colloids should direct the use of crystalloid fluids. It is important to note that excessive diuresis may also lead to a hyper-oncotic state for which crystalloid replacement may be necessary.

See also:

Ovid: Oxford Handbook of Critical Care

Fluids

Crystalloids

Types

- Saline: e.g. 0.9% saline, Ringer's lactate, Hartmann's solution, 0.18% saline in 4% glucose
- Glucose: e.g. 5%, 10%, 20%, 50%
- Sodium bicarbonate: e.g. 1.26%, 8.4%

Uses

- Crystalloid fluids — to provide the daily requirements of water and electrolytes. They should be given to critically ill patients as a continuous background infusion to supplement fluids given during feeding, or to carry drugs.
- Higher concentration glucose infusions — to prevent hypoglycaemia.
- Potassium chloride — to supplement crystalloid fluids.
- Sodium bicarbonate — for correction of metabolic acidosis, urinary alkalinisation, etc

Routes

- IV

Notes

A significant plasma volume deficit should be replaced with colloid solutions since crystalloids are rapidly lost from the plasma, particularly during periods of increased capillary leak, e.g. sepsis. As most plasma substitutes are carried in saline solutions, any additional 0.9% saline crystalloid infusion is only needed to replace excess sodium losses.

The sodium content of 0.9% saline is equivalent to that of extracellular fluid. A daily requirement of 70–80mmol sodium is normal although there may be excess loss in sweat and from the gastrointestinal tract.

Ringer's lactate or Hartmann's solution have no practical advantage over 0.9% saline for fluid maintenance. They

may, however, be useful if large volumes of crystalloid are used to avoid hyperchloraemic acidosis. Hyperchloraemic acidosis may adversly affect coagulation and renal function.

5% glucose is used to supply intravenous water requirements. The 50g/l glucose content ensures an isotonic solution but only provides 200Cal/l. Normal requirement is approximately 1.5–2l/day. Water loss in excess of electrolytes is uncommon but occurs in excess sweating, fever, hyperthyroidism, diabetes insipidus and hypercalcaemia.

Potassium chloride must be given slowly since rapid injection may cause fatal arrhythmias. No more than 40mmol/h should be given although 20mmol/h is more usual. The frequency of infusion is dictated by plasma potassium measurements.

Ion content of crystalloids (mmol/l)

	Na$^+$	K$^+$	HCO3$^-$	Cl$^-$	Ca^{2+}
0.9% saline	150			150	
Hartmann's	131	5	29	111	2
0.18% saline in 4% glucose	30			30	

Ion content of gastrointestinal fluids (mmol/l)

	H$^+$	Na$^+$	K$^+$	HCO3$^-$	Cl$^-$
Gastric	40–60	20–80	5–20	150	100–150
Biliary		120–140	5–15	30–50	80–120
Pancreatic		120–140	5–15	70–110	40–80
Small bowel		120–140	5–15	20–40	90–130
Large bowel		100–120	5–15	20–40	90–130

See also:

Nutrition—use and indications, p78; Urea and creatinine, p144; Electrolytes

$(Na^+, K^+, Cl^-, HCO_3^-)$

, p146; Sodium bicarbonate, p178; Colloids, p180; Hypernatraemia, p416; Hyponatraemia, p418; Hyperkalaemia, p420; Hypokalaemia, p422; Metabolic acidosis, p434; Diabetic ketoacidosis, p442; Hyperosmolar diabetic emergencies, p444; Multiple trauma (1), p500; Multiple trauma (2), p502; Burns—fluid management, p510; Post-operative intensive care, p534

Sodium bicarbonate

Types

- Isotonic sodium bicarbonate 1.26%
- Hypertonic sodium bicarbonate (1mmol/ml) 8.4%

Uses

- Correction of metabolic acidosis.
- Alkalinisation of urine.
- Alkalinisation of blood, e.g. for treatment of tricyclic antidepressant overdose.

Routes

- IV

Notes

Isotonic (1.26%) sodium bicarbonate may be used to correct acidosis associated with renal failure or to induce a forced alkaline diuresis. The hypertonic (8.4%) solution is rarely required in intensive care practice to raise blood pH in severe metabolic acidosis. Bicarbonate therapy is inappropriate when tissue hypoperfusion or necrosis is present.

Administration may be indicated as either specific therapy (e.g. alkaline diuresis for salicylate overdose) or if the patient is symptomatic (usually dyspnoeic) in the absence of tissue hypoperfusion (e.g. renal failure).

The $PaCO_2$ may rise if minute volume is not increased. Bicarbonate cannot cross the cell membrane without dissociation so the increase in $PaCO_2$ may result in intracellular acidosis and depression of myocardial cell function.

The decrease in plasma ionised calcium may also cause a decrease in myocardial contractility. Significantly worse haemodynamic effects have been reported with bicarbonate compared to equimolar saline in patients with severe heart failure.

Convincing human evidence that bicarbonate improves myocardial contractility or increases responsiveness to circulating catecholamines in severe acidosis is lacking, though anecdotal success has been reported. Acidosis relating to myocardial depression is related to intracellular changes that are not accurately reflected by arterial blood chemistry.

Excessive administration may cause hyperosmolality, hypernatraemia, hypokalaemia and sodium overload.

Bicarbonate may decrease tissue oxygen availability by a left shift of the oxyhaemoglobin dissociation curve.

Sodium bicarbonate does have a place in the management of acid retention or alkali loss, e.g. chronic renal failure, renal tubular acidosis, fistulae, diarrhoea. Fluid and/or potassium deficits should be corrected first.

Ion content of sodium bicarbonate (mmol/l)

	Na^+	K^+	$HCO3^-$	Cl^-	Ca^{2+}
1.26% sodium bicarbonate	150		150		
8.4% sodium bicarbonate	1000		1000		

See also:

Blood gas analysis, p100; Electrolytes (Na^+, K^+, Cl^-, HCO_3^-), p146; Crystalloids, p176; Cardiac arrest, p272; Metabolic acidosis, p434; Salicylate poisoning, p454

Colloids

Types

- Albumin: e.g. 4.5–5%, 20–25% human albumin solution
- Dextran: e.g. 6% Dextran 70
- Gelatin: e.g. 3.5% polygeline, 4% succinylated gelatin
- Hydroxyethyl starch: e.g. 6% hetastarch, 6% hexastarch, 6 and 10% pentastarch, 6% tetrastarch

Uses

- Replacement of plasma volume deficit/percentage
- Short term volume expansion (gelatin, dextran)
- Medium term volume expansion (albumin, pentastarch)
- Longer term volume expansion (hetastarch)

Routes

- IV

Side-effects

- Dilution coagulopathy

- Anaphylaxis

- Interference with blood cross-matching (Dextran 70)

Notes

Smaller volumes of colloid are required for resuscitation with less contribution to oedema. Maintenance of plasma colloid osmotic pressure (COP) is a useful effect not seen with crystalloids, but colloids contain no clotting factors or other plasma enzyme systems.

Albumin is the main provider of COP and has several other roles. There is no evidence that maintaining plasma albumin levels, as opposed to plasma COP with artificial plasma substitutes, is better.

Albumin 20–25% and Pentaspan 10% are hyperoncotic and used to provide colloid where salt restriction is necessary. This is rarely necessary in intensive care as plasma volume expansion is related to the weight of colloid infused rather than the concentration. Artificial colloids used with ultrafiltration or diuresis are just as effective in oedema states.

Polygeline is a 3.5% solution containing calcium (6.25mmol/l). This prevents use of the same giving set for blood transfusions. Succinylated gelatin is a 4% solution with a larger molecular size than polygeline giving a slightly longer effect. This, and the lack of calcium in solution, make it more useful than polygeline for short term plasma volume expansion.

In patients with capillary leak albumin and smaller molecular weight colloids leak to the interstitium. In these cases it is perhaps better to use larger molecular weight colloids such as hydroxyethyl starch, though conclusive evidence is lacking.

Hetastarch and hexastarch are usually 6% solutions with a high degree of protection from metabolism due to a high degree of substitution (proportion of glucose units substituted with hydroxyethyl groups—DS) or a high ratio of C2 to C6 carbon atoms substituted (C2:C6 ratio). The molecular weight ranges vary but molecular sizes are large enough to ensure a prolonged effect. These are the most useful colloids in capillary leak. Prolonged itching related to intradermal deposition and interference with coagulation are complications if excessive doses are used.

Pentastarch and tetrastarch provide only a short term effect similar to succinylated gelatin.

Unique features of albumin

- Transport of various molecules.

- Free radical scavenging.

- Binding of toxins.

- Inhibition of platelet aggregation.

Relative persistence of colloid effect

Albumin	+++
Dextran 70	++
Succinylated gelatin	++
Polygeline	+
Hetastarch (high MW, high DS, low C2:C6 ratio)	++++
Hexastarch (medium MW, high DS, high C2:C6 ratio)	++++
Pentastarch (medium MW, low DS, low C2:C6 ratio)	++
Tetrastarch (low MW, low DS, high C2:C6 ratio)	++

- Persistence is dependent on molecular size and protection from metabolism.

- High DS and high C2:C6 ratio protect hydroxyethyl starch from metabolism.

- All artificial colloids are polydisperse (i.e. there is a range of molecular sizes).

Key trial

The SAFE study investigators. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. N Engl J Med 2004; J50:2247-56.

See also:

Blood transfusion

Blood storage

Blood cells are eventually destroyed due to oxidant damage during storage of whole blood. Since white cells and plasma enzyme systems are of importance in this cellular destruction, effects are correspondingly less severe for packed red cells. Blood used for transfusion in most of Europe is now routinely leukodepleted. Microaggregate formation is associated with platelets, white cells and fibrin and range in size from 20–170μm. The risk of microaggregate damage is reduced with packed red cells. In addition to spherocytosis and haemolysis, prolonged storage depletes ATP and 2,3-DPG levels thus increasing the oxygen affinity of the red cells. If whole blood is to be used in critically ill patients it should be as fresh as possible.

Compatibility

In an emergency, with massive blood loss that threatens life, it is permissible to transfuse O negative packed cells but a sample must be taken for grouping prior to transfusion. With modern laboratory procedures it is possible to obtain ABO compatibility for group specific transfusion within 5–10min and a full cross-match in 30min.

Hazards of blood transfusion

- Citrate toxicity—hypocalcaemia is rarely a problem and the prophylactic use of calcium supplementation is not recommended.

- Potassium load—potassium returns to cells rapidly but hyperkalaemia may be a problem if blood is stored at room temperature.

- Sodium load—from citrate if the transfusion is massive.

- Hypothermia—can be avoided by warming blood as it is transfused.

- Jaundice—haemolysis of incompatible or old blood.

- Pyrexia—immunological transfusion reactions to incompatible red or white cells or platelets.

- DIC—partial activation of clotting factors and destruction of stored cells, either in old blood or when transfusion is incompatible.

- Anaphylactoid reaction—urticaria is common and probably due to a reaction to transfused plasma proteins; if severe it may be treated by slowing the transfusion and giving chlorpheniramine 10mg IV/IM. In severe anaphylaxis, in addition to standard treatment, the transfusion should be stopped and saved for later analysis and a sample taken for further cross-matching.

- Transmission of disease—including viruses, parasites (malaria), prions.

- Transfusion-related acute lung injury (TRALI) and other immune reactions.

- A multicentre trial suggested liberal transfusion in the critically ill produced less favourable outcomes, particularly in younger, less sick patients, than using a trigger haemoglobin of 7g/dl.

Key trial

Hebert PC, Wells G, Blajchman MA et al, for the Tranfusion Requirements in Critical Care Investigators. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. N Engl J Med 1999; 340:409–17

See also:

Respiratory drugs

Bronchodilators

Types

- β_2 agonists: e.g. salbutamol, epinephrine, terbutaline
- Anticholinergics: e.g. ipratropium
- Theophyllines: e.g. aminophylline
- Steroids: e.g. hydrocortisone, prednisolone
- Others: e.g. ketamine, isoflurane, halothane

Uses

Relief of bronchospasm

Routes

- Inhaled (salbutamol, epinephrine, terbutaline, ipratropium, isoflurane, halothane)
- Nebulised (salbutamol, epinephrine, terbutaline, ipratropium)
- IV (salbutamol, epinephrine, terbutaline, ipratropium, aminophylline, hydrocortisone, ketamine)
- PO (aminophylline, prednisolone)

Side-effects

- CNS stimulation (salbutamol, epinephrine, terbutaline, aminophylline)
- Tachycardia (salbutamol, epinephrine, terbutaline, aminophylline, ketamine)
- Hypotension (salbutamol, terbutaline, aminophylline, isoflurane, halothane)
- Hyperglycaemia (salbutamol, epinephrine, terbutaline, hydrocortisone, prednisolone)
- Hypokalaemia (salbutamol, epinephrine, terbutaline, hydrocortisone, prednisolone)
- Lactic acidosis (salbutamol)—rare

Notes

Selective β_2 agonists are usually given by inhalation via a pressurised aerosol or a nebulizer. Inhalation often gives rapid relief of bronchospasm, although the aerosol is of less benefit in severe asthma.

Nebulized drugs require a minimum volume of 4ml and a driving gas flow of 6–8l/min.

In extremis, epinephrine may be used IV, SC or injected down the endotracheal tube. As epinephrine is not selective, arrhythmias are more likely. However, the α agonist effect may reduce mucosal swelling by vasoconstriction.

Ipratropium bromide has no systemic effects and does not depress mucocilliary clearance. It is synergistic with β_2 agonists but has a slower onset of action.

Aminophylline is synergistic with β_2 agonists. Dosages must be adjusted according to plasma levels (range 10–20mg/l) since toxic effects may be severe. Dose requirements are reduced by heart failure, liver disease, chronic airflow limitation, fever, cimetidine, erythromycin. Dose requirements are increased in children, smokers and those with a moderate to high alcohol intake.

See also:

Drug dosages

	Aerosol*	Nebuliser*	IV bolus	IV infusion
Salbutamol	100–200µg	2.5–5mg		3–20µg/min
Terbutaline	250–500µg	5–10mg	1.5–5µg/min	
Epinephrine		0.5mg		
Ipratropium		250µg		
Aminophylline			5mg/kg over 20min	0.5mg/kg/h
Hydrocortisone			200mg qds	

*Aerosols and nebulisers are usually given 4–6 times daily but may be given more frequently if necessary.

In extremis, epinephrine may be given as 0.1–0.5mg subcutaneously, injected down the endotracheal tube or by IV infusion.

Respiratory stimulants

Types

- Drug antagonists: e.g. naloxone, flumazenil
- CNS stimulants: e.g. doxapram
- Almitrine

Uses

- Acute respiratory failure due to failure of ventilatory drive.
- Drug induced ventilatory failure, e.g. as a result of excessive sedation or post-operatively.

Routes

- IV

Modes of action

- Naloxone—short acting opiate antagonist.
- Flumazenil—short acting benzodiazepine antagonist.
- Doxapram—generalised central nervous system stimulant with predominant respiratory stimulation at lower doses. Stimulation of carotid chemoreceptors at very low doses with increased tidal volumes.
- Almitrine—increases the sensitivity of carotid chemoreceptors to hypoxaemia and hypercapnia.

Side-effects

- Seizures (flumazenil, doxapram)
- Tachyarrhythmias (naloxone, flumazenil)
- Hallucinations (doxapram)

Notes

Respiratory stimulants are mainly used in patients with chronic airflow limitation who develop acute hypercapnic respiratory failure. Effects of doxapram are short-lived so infusion is necessary. After about 12h infusion the effects on ventilatory drive are reduced.

Naloxone may be used in respiratory depression due to opiate drugs. Since it reverses all opiate effects, it may be better to reverse respiratory depression with non-specific respiratory stimulants, leaving pain relief intact. It may need to be repeated when long acting opiates are involved.

As most benzodiazepines are long acting compared to flumazenil, repeated doses may be necessary.

Almitrine does not produce central respiratory stimulation but it does improve ventilation–perfusion matching by augmenting hypoxic pulmonary vasoconstriction. Effects continue for several hours after injection.

Drug dosages

IV Infusion	IV bolus	IV
Naloxone	0.1–0.4mg	
Flumazenil	0.2mg over 15min (0.1mg/min to max 2mg)	
Doxapram	1–1.5mg/kg over 30s	2–3mg/min
Almitrine	0.25–0.5mg/kg over 30min	

Key paper
Greenstone M, Lasserson TJ. Doxapram for ventilatory failure due to exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2003; CD000223. Review

See also:
Opioid analgesics, p234; Sedatives, p238; Respiratory failure, p282; Sedative poisoning, p458; Post-operative intensive care, p534

Nitric oxide
Nitric oxide is now recognised as a fundamental mediator in many physiological processes. One of its most important effects is smooth muscle relaxation; nitric oxide is the major local controller of vascular tone via effects on cyclic GMP.

Inhaled nitric oxide
Nitric oxide is provided for inhalation from cylinders (1000ppm nitric oxide in nitrogen). It is diluted with inspiratory gases, either at the gas supply to the ventilator or in the inspiratory limb of the ventilator circuit, to provide an inhaled concentration of 1–40ppm, although most patients require less than 20ppm. Inhalation produces vasodilatation at the site of gas exchange, and may improve ventilation–perfusion matching and reduce pulmonary artery pressures. Randomised multi-centre studies in patients with acute lung injury have revealed no long-term benefit or outcome improvement.

Side-effects
Nitric oxide is immediately bound to haemoglobin ensuring local effects only. There is no tolerance but patients can become dependent on continued inhalation with rebound pulmonary hypertension and hypoxaemia on withdrawal. For this reason, withdrawal must be gradual. Excessive humidification of inspired gases may form nitric acid with NO; the use of heat–moisture exchangers rather than water baths is recommended.

Monitoring
Nitric oxide and nitrogen dioxide concentrations may be monitored conveniently with portable fuel cell analysers or by chemiluminescence. It is important to monitor concentrations of both gases in the inspiratory limb of the ventilator circuit. Monitoring of nitrogen dioxide is important to ensure that toxic doses are not formed with the oxygen in the inspired gas and subsequently inhaled by the patient. Although it is extremely rare to see toxic nitrogen dioxide concentrations (>5ppm) it is possible to remove nitrogen dioxide from the inspired gas by using a soda lime adsorber. Methaemoglobin is formed when nitric oxide binds to haemoglobin. Prolonged inhalation at higher doses may rarely produce significant methaemoglobinaemia (>5%) and this should therefore be monitored daily.

Achieving the correct dose
Approximately 50% of patients with severe respiratory failure respond to nitric oxide. However, the most effective dose varies. It is usual to start at 1ppm for 10min and monitor the change in PaO_2/FIO_2 ratio. An increase should be followed by an increase in nitric oxide concentration to 5ppm for a further 10min. Thereafter, the dose is adjusted according to response at 10min intervals until the most effective dose is found. Since the underlying pathophysiology may change, it is important to assess the dose response at daily intervals, aiming to keep the dose at the lowest effective level.

Scavenging
Since the concentrations used are so small, dilution of exhaled gases into the atmosphere is unlikely to produce important environmental concentrations. In the air-conditioned intensive care environment air changes are so

frequent as to make scavenging unnecessary.

Key trials

Dellinger RP et al, for the Inhaled Nitric Oxide in ARDS Study Group. Effects of inhaled nitric oxide in patients with acute respiratory distress syndrome: results of a randomized phase II trial. Crit Care Med 1998; 26:15–23

Lundin S et al, for the The European Study Group of Inhaled Nitric Oxide. Inhalation of nitric oxide in acute lung injury: results of a European multicentre study. Intensive Care Med 1999; 25:911–19

See also:

Surfactant

In ARDS there is decreased surfactant production, biochemical abnormality of the surfactant produced and inhibition of surfactant function. The net result is alveolar and small airway collapse. Surfactant also contributes to host defence against micro-organisms. Surfactant replacement would be expected to exert therapeutic effects on lung mechanics, gas exchange and host defence.

Instillation of surfactant (either as a liquid or nebulised) via the endotracheal tube into the lungs is associated with improved outcome in neonatal respiratory distress syndrome. Potential indications in adults include ARDS, pneumonia, chronic airflow limitation and asthma. Multiple studies in ARDS have yet to demonstrate mortality benefit, though this may be related to the type of surfactant, the volume used, or the delivery system.

Studies have demonstrated improved oxygenation with recombinant surfactant protein C and a trend to improved survival in patients with direct lung injury. Further studies are underway using recombinant surfactant protein C with phospholipids, and with surfactant proteins B and C. The surfactant is instilled into the lungs via an endotracheal catheter.

Complications of surfactant treatment have included increased cough, sputum production, bronchospasm, increasd peak airway pressure and adverse effects on pulmonary function. These can be minimised by adequate sedation and neuromuscular blockade before instilling surfactant.

Key trial

Spragg RG, Lewis JF, Walmrath HD et al. Effect of recombinant surfactant protein C-based surfactant on the acute respiratory distress syndrome. N Engl J Med 2004; 351:884–92

See also:

Ovid: Oxford Handbook of Critical Care

Cardiovascular Drugs

Inotropes

Types

- Catecholamines: e.g. epinephrine, norepinephrine, dobutamine, dopamine

- Phosphodiesterase (PDE) inhibitors: e.g. milrinone, enoximone

- Dopexamine

- Calcium sensitisers: e.g. levosimendan

- Cardiac glycosides: e.g. digoxin (weak)

Modes of action

- Increase force of myocardial contraction, either by stimulating cardiac β_1 adrenoreceptors (catecholamines), decreasing cAMP breakdown (PDE inhibitors), increasing calcium sensitivity (Ca sensitisers), directly increasing contractility (digoxin), or inhibiting neuronal reuptake of noradrenaline (dopexamine). All agents except digoxin

have, to greater or lesser degrees, associated dilator or constrictor properties via β_1 and β_1 adrenoreceptors, dopaminergic receptors, or K_{ATP} channels.

- Digoxin may cause splanchnic vasoconstriction and, for an inotropic effect, requires plasma levels at the top of the therapeutic range.
- The increase in cardiac work is partially offset in those drugs possessing associated dilator effects.
- Other than epinephrine (when used for its vasoconstrictor effect in cardiopulmonary resuscitation) or digoxin (for long term use in chronic heart failure), inotropes are usually given by continuous IV infusion titrated for effect.

Uses

- Myocardial failure, e.g. post-myocardial infarction, cardiomyopathy
- Myocardial depression, e.g. sepsis
- Augmentation of oxygen delivery in high-risk surgical patients

Side-effects

- Arrhythmias (usually associated with concurrent hypovolaemia)
- Tachycardia (usually associated with concurrent hypovolaemia)
- Hypotension (related to dilator properties ± concurrent hypovolaemia)
- Hypertension (related to constrictor properties)
- Anginal chest pain, or ST-segment and T-wave changes on ECG

Notes

Epinephrine, norepinephrine, dobutamine and dopamine should be given via a central vein as tissue necrosis may occur secondary to peripheral extravasation.

Drug dosages

Epinephrine	Infusion starting from 0.05µg/kg/min
Norepinephrine	Infusion starting from 0.05µg/kg/min
Dobutamine	Infusion from 2.5–25µg/kg/min
Dopamine	Infusion from 2.5–50µg/kg/min
Dopexamine	Infusion from 0.5–6µg/kg/min
Milrinone	Loading dose of 50µg/kg over 10min followed by infusion from 0.375–0.75µg/kg/min
Enoximone	Loading dose of 0.5–1mg/kg over 10min followed by infusion from 5–20µg/kg/min
Digoxin	0.5mg given PO or IV over 10–20min. Repeat at 4–8h intervals until loading achieved (assessed by clinical response). Maintenance dose thereafter is 0.0625–0.25mg/day depending on plasma levels and clinical response.
Levosimendan	12–24µg/kg over 10min followed by 0.1µg/kg/min for 24h

See also:

Vasodilators

Types

- Nitrates: e.g. glyceryl trinitrate, isosorbide dinitrate
- Angiotensin converting enzyme (ACE) inhibitors: e.g. captopril
- Smooth muscle relaxants: e.g. sodium nitroprusside, hydralazine
- α-adrenergic antagonists: e.g. phentolamine
- β_2-adrenergic agonists: e.g. salbutamol
- Calcium antagonists: e.g. nifedipine, diltiazem
- Dopaminergic agonists: e.g. dopexamine
- Phosphodiesterase inhibitors: e.g. enoximone, milrinone, sildenafil
- Prostaglandins: e.g. epoprostenol (PGI_2), alprostadil (PGE_1)
- B-type natriuretic peptide analogues, e.g. nesiritide

Modes of action

- Increase cyclic GMP concentration (by nitric oxide donation or by inhibiting cGMP breakdown), or acts directly on dopaminergic receptors leading to vasodilatation
- Reduce (to varying degrees) ventricular preload and/or afterload.
- Reduce cardiac work.

Uses

- Myocardial failure, e.g. post-myocardial infarction, cardiomyopathy
- Angina/ischaemic heart disease
- Systemic hypertension (specific causes, e.g. phaeochromocytoma)
- Vasoconstriction
- Peripheral vascular disease/hypoperfusion
- Splanchnic perfusion (dopexamine, dopamine)
- Pulmonary hypertension (inhaled NO, prostaglandins, sildenafil)

Side-effects/complications

- Hypotension (often associated with concurrent hypovolaemia)
- Tachycardia (often associated with concurrent hypovolaemia)
- Symptoms include headache, flushing, postural hypotension
- Renal failure (ACE inhibitors)—especially with renal artery stenosis, hypovolaemia, non-steroidals

Notes

Glyceryl trinitrate and isosorbide dinitrate reduce both preload and afterload. At higher dose the afterload effect becomes more prominent.

Tolerance to nitrates usually commences within 24–36h unless intermittent oral dosing is used. Progressive increases in dose are required to achieve the same effect.

Prolonged (>24–36h) dose-related administration of sodium nitroprusside can rarely produce a metabolic acidosis related to cyanide accumulation.

ACE inhibitor tablets can be crushed and given either SL or via a nasogastric tube.

Dopaminergic drugs improve splanchnic blood flow though clinical benefits are unproved.

Hydralazine has an unpredictable effect on blood pressure and, if given IV, should be used with caution.

Drug dosages

Nitrates	Glyceryl trinitrate 2–40mg/h Isosorbide dinitrate 2–40mg/h

Sodium nitroprusside	20–400µg/min
Hydralazine	5–10mg by slow IV bolus, repeat after 20–30min. Alternatively, by infusion starting at 200–300µg/min and reducing to 50–150µg/min
ACE inhibitors	Captopril: 6.25mg test dose increasing to 25mg tds Enalapril: 2.5mg test dose increasing to 40mg od Lisinopril: 2.5mg test dose increasing to 40mg od
Nifedipine:	5–20mg PO. Capsule fluid can be injected down nasogastric tube or given sublingually
Phentolamine	2–5mg IV slow bolus. Repeat as necessary.
Dopexamine	Infusion from 0.5–6µg/kg/min
Milrinone	Loading dose of 50µg/kg over 10min followed by infusion from 0.375–0.75µg/kg/min
Enoximone	Loading dose of 0.5–1mg/kg over 10min followed by infusion from 5–20µg/kg/min
Epoprostenol, alprostadil	Infusion from 2–30ng/kg/min
Nitric oxide	By inhalation: 2–40ppm
Nesiritide	2µg/kg bolus followed by infusion of 0.01–0.03µg/kg/min
Sildenafil	50mg tds PO

See also:

Vasopressors

Types

- α-adrenergic: e.g. norepinephrine, epinephrine, dopamine, ephedrine, phenylephrine, methoxamine
- Drugs reducing production of cyclic GMP (in septic shock): e.g. methylthioninium chloride (methylene blue)
- Vasopressin or synthetic analogues, e.g. terlipressin

Modes of action

- Acting on peripheral α-adrenergic or vasopressin V1 receptors
- Blocking cGMP production (methylene blue)
- Increase afterload, mainly by arteriolar vasoconstriction and restoration of vascular reactivity
- Venoconstriction

Uses

- To increase organ perfusion pressures, particularly in high output, low peripheral resistance states, e.g. sepsis, anaphylaxis
- To raise coronary perfusion pressures in cardiopulmonary resuscitation (epinephrine, vasopressin)

Side-effects/complications

- Increased cardiac work
- Decreased cardiac output, especially with agents where pressor effects predominate
- Myocardial and splanchnic ischaemia
- Increased myocardial irritability, especially with concurrent hypovolaemia, leading to arrhythmias and tachycardia
- Decreased peripheral perfusion and distal ischaemia/necrosis

Notes

Pressor agents should be avoided, if possible, in low cardiac output states as they may further compromise the circulation.

Methoxamine and phenylephrine are the 'purest' pressor agents; other α-adrenergic agents have inotropic properties to greater or lesser degrees. Ephedrine is similar to epinephrine but its effects are more prolonged as it is not metabolised by monoamine oxidase.

Effects of pressor agents on splanchnic, renal and cerebral circulations are variable and unpredictable.

Pulmonary vascular resistance is also raised by these agents.

Methylthioninium chloride (methylene blue) inhibits the NO–cGMP pathway. It is currently unlicensed as a pressor agent and its use has only been reported in a few small case series. A multicentre study of a NO synthase inhibitor (L-NMMA) was prematurely discontinued due to adverse outcomes.

Vasopressin (short half-life, infusion needed) and terlipressin (longer half-life, can be given by bolus) may be effective in treating catecholamine-resistant vasodilatory shock. Paradoxically, such patients respond to small doses that have no pressor effect in healthy people. Multicentre outcome studies are ongoing.

Excessive dosing of any pressor agent may lead to regional ischaemia, e.g. cardiac, splanchnic. Digital ischaemia may respond to prompt administration of intravenous prostanoids (e.g. PGE_1, PGI_2).

Drug dosages

Norepinephine	Infusion starting from 0.05µg/kg/min
Epinephrine	Infusion starting from 0.05µg/kg/min
Dopamine	Infusion from 5–50µg/kg/min
Methoxamine	3–10mg by slow IV bolus (rate of 1mg/min)
Ephedrine	3–30mg by slow IV bolus
Methylthioninium chloride (methylene blue)	1–2mg/kg over 15–30min
Vasopressin	0.01–0.04U/min
Terlipressin	0.25–0.5mg bolus, repeated at 30min intervals as necessary to maximum 2mg.

Key paper

Lopez A, et al. Multiple-center, randomized, placebo-controlled, double-blind study of the nitric oxide synthase inhibitor 546C88: effect on survival in patients with septic shock. Crit Care Med 2004; 32:21–30

Landry DW, et al. Vasopressin deficiency contributes to the vasodilation of septic shock. Circulation 1997; 95:1122–5

Hypotensive agents

Types

- Vasodilators

- α- and β-adrenergic blockers

- In routine ICU practice β-blockers are used relatively infrequently because most have a long half-life and the negative inotropic effects are generally undesirable. Exceptions are esmolol and labetalol, both of which have short half-lives and vasodilating properties.

Modes of action

- Vasodilators reduce preload and afterload to variable degrees depending on type and dose

- β-blockers reduce the force of myocardial contractility

Uses

- Hypertension—systemic and pulmonary

- Heart failure—to reduce afterload ± preload (caution with β-blockers)

- Control of blood pressure, e.g. dissecting aortic aneurysm

Side-effects/complications

- Excessive hypotension

- Heart failure (with β-blockers)

- Peripheral hypoperfusion (with β-blockers)

- Bronchospasm (with β-blockers)

- Decreased sympathetic response to hypoglycaemia (with β-blockers)

Notes

In critically ill patients it is often advisable to use short-acting β-blockers by infusion.

Drug dosages

Nitrates	Glyceryl trinitrate 2–40mg/h
	Isosorbide dinitrate 2–40mg/h
Sodium nitroprusside	20–400µg/min.
ACE inhibitors	Captopril: 6.25mg test dose increasing to 25mg tds
	Enalapril: 2.5mg test dose increasing to 40mg o.d
	Lisinopril: 2.5 mg test dose increasing to 40mg o.d
Nifedipine:	5–20mg PO. Capsule fluid can be injected down nasogastric tube or given sublingually.
Phentolamine	2–5mg IV slow bolus. Repeat as necessary
Esmolol	A titrated loading dose regimen is commenced followed by an infusion rate of 50–200µg/kg/min.
Propranolol	Initially given as slow IV 1mg boluses repeated at 2min intervals until effect is seen (to maximum 5mg)
Labetalol	0.25–2mg/min
Hydralazine	5–10mg by slow IV bolus, repeat after 20–30min. Alternatively, by infusion starting at 200–300µg/min and reducing to 50–150µg/min.

See also:

Antiarrhythmics

Only antiarrhythmics likely to be used in the ICU setting are described.

For supraventricular tachyarrhythmias:

adenosine, verapamil, amiodarone, digoxin, β-blockers, magnesium

For ventricular tachyarrhythmias:

amiodarone, lidocaine, flecainide, bretylium, β-blockers, magnesium

Uses

- Correction of supraventricular and ventricular tachyarrhythmias which either compromise the circulation or could potentially do so.
- Differentiation between supraventricular and ventricular arrhythmias using adenosine

Notes

All antiarrhythmic agents have side-effects; other than digoxin they are negatively inotropic to greater or lesser degrees and may induce profound hypotension (e.g. verapamil, β-blockers) or bradycardia (e.g. β-blockers, amiodarone, digoxin, lidocaine). β-blockers in particular should be used with caution because of these effects.

All A-V blockers are contraindicated in re-entry tachycardia (e.g. Wolff–Parkinson–White syndrome).

- Adenosine: very short-acting; may revert paroxysmal SVT to sinus rhythm. Ineffective for atrial flutter and fibrillation, VT. Contraindicated in 2° and 3° heart block, sick sinus syndrome, asthma. May cause flushing, bronchospasm and occasional severe bradycardia.

- Amiodarone: effective against all types of tachyarrhythmia. Usually given by IV infusion for rapid effect but requires initial loading dose. When converting from IV to oral dosing, initial high oral dosing (200mg tds) is still required. Contraindicated in patients with thyroid dysfunction. Has low acute toxicity, though may cause severe bradycardia and both chronic and acute pulmonary fibrosis. Avoid with other Class III agents (e.g. sotalol). Must be given via central vein as causes peripheral phlebitis.

- β-blockers: for SVT, esmolol is preferred due to its short half-life though may cause vasodilatation. Initially, increasing loading doses required; an infusion may be needed thereafter. Propranolol can be given by slow IV boluses of 1mg repeated at 2min intervals to a maximum of 5mg). Do not give β-blockers with verapamil.

- Bretylium: may take 15–20min to take effect; now used predominantly for resistant VF/VT. CPR should be continued for at least 20min.

- Digoxin: slow-acting, requires loading (1–1.5g) to achieve therapeutic plasma levels which can be monitored. Loading ideally given over 12–24h but can be done over 4–6h. Contraindicated in 2° and 3° heart block. May cause severe bradycardia. Low K^+ and Mg^{2+} and markedly raised Ca^{2+} increase myocardial sensitivity to digoxin. Amiodarone raises digoxin levels.

- Lidocaine: 10ml of 1% solution contains 100mg. No effect on SVT. Loading achieved by 1mg/kg slow IV bolus followed by infusion. Contraindicated in 2° and 3° heart block. May cause bradycardia and CNS side-effects, e.g. drowsiness, seizures.

- Verapamil: should not be given with β-blockers as profound hypotension and bradyarrhythmias may result. Pretreatment with 3–5ml 10% calcium gluconate by slow IV bolus prevents the hypotensive effects of verapamil without affecting its antiarrhythmic properties.

Modes of action (Vaughan-Williams classification)

Class	Action	Examples
I	Reduces rate of rise of action potential:	
	•Ia: increases action potential duration	•Ia: disopyramide
	•Ib: shortens duration	•Ib: lidocaine
	•Ic: little effect	•Ic: flecainide
II	Reduces rate of pacemaker discharge	β-blockers
III	Prolongs duration of action potential and hence length of refractory period	Amiodarone
		Sotalol
IV	Antagonises transport of calcium across cell membrane	Verapamil Diltiazem

Drug dosages

Adenosine	3mg rapid IV bolus. If no response after 1min give 6mg. If no response after 1min give 12mg.
Amiodarone	5mg/kg over 20min (or 150–300mg over 3min in emergency) then IV infusion of 15mg/kg/24h in 5% glucose via central vein. Reduce thereafter to 10mg/kg/24h (approx. 600mg/day) for 3–7 days then maintain at 5mg/kg/24h (300–400mg/day)
β-blockers	Esmolol: a titrated loading dose regimen is commenced followed by an infusion rate of 50–200µg/kg/min.
	Propranolol: Initially given as slow IV boluses of 1mg repeated at 2min intervals until effect is seen to a maximum of 5mg.
	Labetalol: 0.25–2mg/min
Bretylium	In emergency 5mg/kg by rapid IV bolus. If no response after 5min, repeat or increase to 10mg/kg.
Digoxin	0.5mg given IV over 10–20min. Repeat at 4–8h intervals until loading achieved (assessed by clinical response). Maintenance dose thereafter is 0.0625–0.25mg/day depending on plasma levels and clinical response.
Lidocaine	1mg/kg slow IV bolus for loading then 2–4mg/min infusion. Should be weaned slowly over 24h.
$MgSO_4$	10–20mmol over 1–2h. Can be given over 5min in emergency.
Verapamil	2.5mg slow IV. If no response repeat to a maximum of 20mg. An IV infusion of 1–10mg/h may be tried. 10% calcium gluconate solution should be readily available.

See also:

Defibrillation, p52; ECG monitoring, p108; Basic resuscitation, p270; Cardiac arrest, p272; Tachyarrhythmias

Chronotropes

Types

- Anticholinergic: e.g. atropine, glycopyrrolate

Modes of action

- The anticholinergic drugs act by competitive antagonism of acetylcholine at peripheral muscarinic receptors and decrease atrioventricular conduction time.

Uses

- All types of bradycardia including 3° heart block.
- High dose atropine is used in cardiopulmonary resuscitation protocols for treatment of asystole.

Side-effects/complications

- Anticholinergic drugs produce dry mouth, reduction and thickening of bronchial secretions, and inhibition of sweating. Urinary retention may occur but parenteral administration does not lead to glaucoma.

Notes

The anticholinergic agents are usually given by IV bolus, repeated as necessary.

They are frequently used as a bridge to temporary pacing but should not be considered a substitute. External or internal pacing should be readily accessible.

Atropine nebulisers have been used successfully in patients developing symptomatic bradycardia during endotracheal suction.

Neurological effects may be seen with atropine but not glycopyrrolate.

Drug dosages

Atropine	0.3–0.6mg IV bolus. 3mg is needed for complete vagal blockade.
Glycopyrrolate	0.2–0.4mg IV bolus.

See also:

Temporary pacing (1), p54; Temporary pacing (2), p56; ECG monitoring, p108; Basic resuscitation, p270; Cardiac arrest, p272; Bradyarrhythmias, p318

Antianginal agents

Types

- Vasodilators: e.g. nitrates, calcium antagonists
- β-blockers
- Potassium channel openers: e.g. nicorandil
- Aspirin, heparin, clopidogrel

Modes of action

- Calcium channel blockers cause competitive blockade of cell membrane and slow calcium channels leading to decreased influx of calcium ions into cells. This leads to inhibition of contraction and relaxation of cardiac and smooth muscle fibres resulting in coronary and systemic vasodilatation.
- Nitrates may cause efflux of calcium ions from smooth muscle and cardiac cells and also increase cGMP synthesis resulting in coronary and systemic vasodilatation.
- β-blockers inhibit β-adrenoreceptor stimulation, reducing myocardial work and oxygen consumption. This effect is somewhat offset by compensatory peripheral vasoconstriction.
- Potassium channel openers cause vasodilatation by relaxation of vascular smooth muscle. The potassium channel opening action works on the arterial circulation while a nitrate action provides additional vasodilatation.
- Though aspirin, heparin and clopidogrel have no direct antianginal effect, patients with unstable angina benefit from the reduction in platelet aggregation and thrombus formation.

Uses

- Angina pectoris

Side-effects/complications

- See Dilators, Hypotensive agents.
- Nicorandil is contraindicated in hypotension and cardiogenic shock. It should be avoided in hypovolaemia. Headache and flushing are the major reported side-effects. Rapid and severe hyperkalaemia has been reported after cardiac surgery.

Notes

Combination therapy involving intravenous nitrates, calcium antagonists, β-blockade and heparinisation has been shown to be beneficial in unstable angina; thrombolytic therapy confers no added advantage.

Potassium channel openers belong to a new class of drug yet to be extensively evaluated in critically ill patients and should be thus used with caution, especially when hyperkalaemia is a concern.

Angina may occasionally be worsened by a 'coronary steal' phenomenon where blood flow is diverted away from stenosed coronary vessels. This does not, however, occur with nicorandil.

Drug dosages

Glyceryl trinitrate	0.3mg sublingually, 0.4–0.8mg by buccal spray, 2–40mg/h by IV infusion.
Isosorbide dinitrate	10-20mg tds orally, 2–40mg/h by IV infusion.
Nifedipine	5–20mg PO. The capsule fluid can be aspirated then injected down nasogastric tube or given sublingually.
Propranolol	Given either orally at doses of 10–100mg tds or IV as slow boluses of 1mg repeated at 2min intervals to a maximum of 5mg until effect is seen. This can be repeated every 2–4h as necessary.
Nicorandil	10–20mg PO bd.
Clopidogrel	75mg PO od.
Aspirin	75–150mg PO od.

See also:

Renal Drugs

Diuretics

Types

- Loop diuretics: e.g. furosemide, bumetanide
- Osmotic diuretics: e.g. mannitol
- Thiazides: e.g. metolazone
- Potassium sparing diuretics: e.g. amiloride, spironolactone, potassium canrenoate

Uses

- To increase urine volume
- Control of chronic oedema (thiazides, loop diuretics)
- Control of hypertension (thiazides)
- To promote renal excretion (e.g. forced diuresis, hypercalcaemia)

Routes

- IV (mannitol, furosemide, bumetanide, potassium canrenoate)
- PO (metolazone, furosemide, bumetanide, amiloride, spironolactone)

Modes of action

- Osmotic diuretics—reduce distal tubular water reabsorption

- Thiazides—inhibit distal tubular Na^+ loss and carbonic anhydrase and increase Na^+ and K^+ exchange. This reduces the supply of H^+ ions for exchange with Na^+ ions producing and alkaline natriuresis with potassium loss

- Loop diuretics—inhibit Na^+ and Cl^- reabsorption in the ascending loop of Henlé

- Potassium sparing diuretics—inhibit distal tubular Na^+ and K^+ exchange

Side-effects

- Hypovolaemia

- Hyponatraemia or hypernatraemia

- Hypokalaemia

- Oedema formation (mannitol)

- Reduced catecholamine effect (thiazides)

- Hyperglycaemia (thiazides)

- Metabolic alkalosis (loop diuretics)

- Hypomagnesaemia (loop diuretics)

- Pancreatitis (furosemide)

Notes

It is important to correct pre-renal causes of oliguria before resorting to diuretic use.

Diuretics do not prevent renal failure but may convert oliguric to polyuric renal failure.

If there is inadequate glomerular filtration, mannitol is retained and passes to the extracellular fluid to promote oedema formation.

Bumetanide may be used in porphyria where thiazides and other loop diuretics are contraindicated.

Potassium sparing diuretics should be avoided with ACE inhibitors as there is an increased risk of hyperkalaemia.

Drug dosages

	Oral	IV	Infusion
Mannitol		100g over 20min 6-hrly	
Metolazone	5–10mg od		
Furosemide	20–40mg 6–24-hrly	5–80mg 6–24-hrly	1–10mg/h
Bumetanide	0.5–1mg 6–24-hrly	0.5–2mg 6–24-hrly	1–5mg/h
Amiloride	5–10mg 12–24-hrly		
Spironolactone	100–400mg od		
K^+ canrenoate		200–400mg od	

Dopamine

The effects of dopamine are dependent on the dose infused. Dopamine was used widely at low doses in an attempt to secure preferential DA_1 stimulation and increase renal perfusion; however, a large multicentre randomised controlled study comparing 'renal dose' dopamine and diuretics showed no difference in the incidence of renal failure. The widespread use of low dose dopamine ($<3\mu g/kg/min$) has thus diminished considerably in recent years. Higher doses increase cardiac contractility via β_1 stimulation and produce vasoconstriction via α stimulation. Where vasoconstriction is inappropriate this will reduce renal perfusion. There is, however, evidence of natriuresis and diuresis by enhanced Na^+ transport in the ascending loop of Henlé. This effect is similar to that of a loop diuretic. In addition to the renal effects of DA_1 stimulation there may be preferential perfusion of the splanchnic bed, though any benefits to patients have yet to be shown.

Key trial

Bellomo R, for the Australian and New Zealand Intensive Care Society (ANZICS) Clinical Trials Group. Low-dose dopamine in patients with early renal dysfunction: a placebo-controlled randomised trial. Lancet 2000; 356:2139–43

See also:

Ovid: Oxford Handbook of Critical Care

Gastrointestinal Drugs

H$_2$ blockers and proton pump inhibitors

Types

- H$_2$ antagonists: e.g. ranitidine, cimetidine
- Proton pump inhibitors: e.g. omeprazole

Modes of action

These agents inhibit secretion of gastric acid, reducing both volume and acid content, either by antagonism of the histamine H$_2$ receptor or by inhibiting H$^+$K$^+$-ATPase which fuels the parietal cell proton pump on which acid secretion depends.

Uses

- Peptic ulceration, gastritis, duodenitis
- Reflux oesophagitis
- Prophylaxis against stress ulceration
- Upper gastrointestinal haemorrhage of peptic/stress ulcer origin
- With non-steroidal anti-inflammatory agents in patients with dyspepsia
- Gastric tonometry measurement

Side-effects/complications

- The major concern voiced against these agents is the increased risk of nosocomial pneumonia by removal of the acid barrier. However, a multicentre RCT comparing ranitidine with sucralfate showed no difference in pneumonia rate and a lower incidence of GI bleeding.
- H$_2$ antagonists: rare but include arrhythmias, altered liver function tests, confusion (in the elderly).
- Proton pump inhibitors: altered liver function tests.

Notes

Although licensed and frequently used for stress ulcer prophylaxis, overwhelming supportive evidence is scanty. Enteral nutrition has been shown to be as effective. No adequately powered study of proton pump inhibitors has yet been performed in ICU patients.

Some studies have shown efficacy in upper gastrointestinal haemorrhage secondary to stress ulceration or peptic ulceration.

Dosages should be modified in renal failure.

Cimetidine can affect metabolism of other drugs, in particular warfarin, phenytoin, theophylline and lidocaine (related to hepatic cytochrome P450-linked enzyme systems). This does not occur with ranitidine.

Omeprazole can delay elimination of diazepam, phenytoin and warfarin.

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Drug dosages

Ranitidine	50mg tds by slow IV bolus, 150mg bd PO
Cimetidine	200–400mg qds by slow IV bolus, 400mg bd PO
Omeprazole	40mg IV od (over 20–30min), 20–40mg PO

Key trial

Cook D, Guyatt G, Marshall J, et al. A comparison of sucralfate and ranitidine for the prevention of upper gastrointestinal bleeding in patients requiring mechanical ventilation. Canadian Critical Care Trials Group. N Engl J Med 1998; 338:791–7

See also:

Sucralfate

Modes of action

- Sucralfate is a basic aluminium salt of sucrose octasulphate and is probably not absorbed from the gastrointestinal tract.
- Exerts a cytoprotective effect by preventing mucosal injury. A protective barrier is formed both over normal mucosa and any ulcer lesion providing protection against penetration of gastric acid, bile and pepsin as well as irritants such as aspirin and alcohol.
- Directly inhibits pepsin activity and absorbs bile salts.
- Weak antacid activity.

Uses

- Peptic ulceration, gastritis, duodenitis
- Reflux oesophagitis
- Prophylaxis against stress ulceration

Side-effects/complications

- Constipation
- Reduced bioavailability of some drugs given orally, e.g. digoxin, phenytoin. Can be overcome by giving agents at least 2h apart.
- Use with caution in renal failure due to risk of increased aluminium absorption.

Notes

Although licensed and frequently used for stress ulcer prophylaxis, overwhelming supportive evidence is scanty. Enteral nutrition and gastric acid blockers have been shown to be as effective.

Evidence for a reduced incidence of nosocomial pneumonia compared to H_2 blocker therapy is also conflicting. Significant reduction in nosocomial pneumonia has been shown compared to a combination of H_2 blocker plus antacid but not against H_2 blocker alone. Indeed, a large multicentre RCT comparing ranitidine with sucralfate showed no difference in pneumonia rate and a lower incidence of GI bleeding with ranitidine.

Antacids should not be given for 30min before or after sucralfate.

Drug dosages

| Sucralfate | 1g six times a day PO or via ng tube. |

Key trial

Cook D, Guyatt G, Marshall J, et al. A comparison of sucralfate and ranitidine for the prevention of upper gastrointestinal bleeding in patients requiring mechanical ventilation. Canadian Critical Care Trials Group. N Engl J Med 1998; 338:791–7

See also:

Antacids

Types

- Sodium bicarbonate
- Magnesium-based antacids: e.g. magnesium trisilicate
- Aluminium-based antacids: e.g. aluminium hydroxide (Aludrox)
- Proprietary combinations: e.g. Gaviscon

Modes of action

- Neutralises gastric acid
- Provides protective coating on upper gastrointestinal mucosa

Uses

- Symptomatic relief of gastritis, duodenitis, oesophagitis
- Stress ulcer prophylaxis (contentious)

Side-effects/complications

- Possible increased risk of nosocomial pneumonia
- Aluminium toxicity (if aluminium-containing antacids are used long-term in patients with renal dysfunction)
- Diarrhoea (magnesium-based antacids)
- Constipation (aluminium-based antacids)
- Metabolic alkalosis if large amounts are administered
- Milk-alkali syndrome resulting in hypercalcaemia, metabolic alkalosis and renal failure is very rare

Notes

As their main use is for symptomatic relief, antacids are rarely needed in mechanically ventilated patients.

Continual nasogastric infusion of a weak sodium bicarbonate solution has been used successfully in treating stress ulcer-related haemorrhage.

Drug dosages

Magnesium trisilicate	10–30ml qds
Aluminium hydroxide	10–30ml qds
Gaviscon	10–30ml qds

See also:

Upper gastrointestinal endoscopy, p74; H_2 blockers and proton pump inhibitors, p218; Sucralfate, p220; Upper gastrointestinal haemorrhage, p344; Bleeding varices, p346; Bowel perforation and obstruction, p348

Anti-emetics

Types

- Phenothiazines: e.g. prochlorperazine, chlorpromazine
- Benzamides: e.g. metoclopramide
- Antihistamines: e.g. cyclizine
- $5HT_3$ receptor antagonists: e.g. ondansetron, granisetron

Modes of action

- Phenothiazines increase the threshold for vomiting at the chemoreceptor trigger zone via central DA_2-dopaminergic blockade; at higher doses there may also be some effect on the vomiting centre.
- Metoclopramide acts centrally and by increasing gastric motility.
- The exact mechanism of cyclizine action is unknown. It increases lower oesophageal sphincter tone and may inhibit the midbrain emetic centre.
- Ondansetron is a highly selective $5HT_3$ receptor antagonist; its precise mode of action is unknown but may act both centrally and peripherally.

Uses

- Nausea
- Vomiting

Side-effects/complications

- Dystonic or dyskinetic reactions, oculogyric crises (prochlorperazine, metoclopramide)
- Arrhythmias (metoclopramide, prochlorperazine)
- Headaches, flushing (ondansetron)
- Urticaria, drowsiness, dry mouth, blurred vision, urinary retention (cyclizine)
- Postural hypotension (prochlorperazine, cyclizine)
- Rarely, neuroleptic malignant syndrome (prochlorperazine, metoclopramide)

Notes

The initial choice should fall between prochlorperazine, metoclopramide or cyclizine. Prochlorperazine and cyclizine are preferable when vomiting is related to drugs and metabolic disturbances acting at the chemoreceptor trigger zone while metoclopramide should be tried first if a gastrointestinal cause is implicated.

Metoclopramide and prochlorperazine dosage should be reduced in renal and hepatic failure.

Ondansetron dosage should be reduced in hepatic failure.

Drug dosages

Prochlorperazine	5–10mg tds PO, 12.5mg qds IM or by slow IV bolus (note: not licensed for IV use)
Metoclopramide	10mg tds by slow IV bolus, IM or PO
Cyclizine	50mg tds slow IV bolus, IM or PO
Ondansetron	4–8mg tds by slow IV bolus, IM or PO
Granisetron	1–3mg by slow IV bolus up to max 9mg/24h

See also:

Enteral nutrition, p80; Vomiting/gastric stasis, p338

Gut motility agents

Types

- Metoclopramide
- Erythromycin

Modes of action

- Metoclopramide probably acts by blocking peripheral DA_2-dopaminergic receptors
- Erythromycin is a motilin agonist acting on antral enteric neurones

Uses

- Ileus, large nasogastric aspirates
- Vomiting

Side-effects/complications

- Dystonic or dyskinetic reactions, oculogyric crises (metoclopramide)
- Arrhythmias (metoclopramide and erythromycin)
- Cholestatic jaundice (erythromycin)

Notes

Metoclopramide dosing should be reduced in renal failure and hepatic failure, while erythromycin dosing should be reduced in hepatic failure.

Drug dosages

Metoclopramide	10mg tds by slow IV bolus, IM or PO
Erythromycin	250mg qds PO or IV

See also:

Enteral nutrition, p80; Vomiting/gastric stasis, p338; Bowel perforation and obstruction, p348

Antidiarrhoeals

Types

- Loperamide
- Codeine phosphate

Modes of action

Loperamide and codeine phosphate bind to gut wall opiate receptors, reducing propulsive peristalsis and increasing anal sphincter tone

Side-effects/complications

- Abdominal cramps, bloating
- Constipation (if excessive amounts given)

Notes

Should not be used when abdominal distension develops, particularly with ulcerative colitis or pseudomembranous colitis, or as sole therapy in infective diarrhoea.

Caution with loperamide in liver failure, and codeine in renal failure.

Drug dosages

Loperamide	2 capsules (20ml) initially, then 1 capsule (10ml) after every loose stool for up to 5 days
Codeine phosphate	30–60mg 4–6hrly PO, IM or by slow IV bolus

See also:

Enteral nutrition, p80; Diarrhoea, p340

Anticonstipation agents

Types

- Laxatives: e.g. lactulose, propantheline, mebeverine, castor oil
- Bulking agents: e.g. dietary fibre (bran), hemicelluloses (methylcellulose, ispaghula husk)
- Suppositories: e.g. glycerine
- Enemata: e.g. warmed normal saline, olive oil or arachis oil retention enemata

Modes of action

- Laxatives include
  i. antispasmodic agents such as anticholinergics (e.g. propantheline) and mebeverine (a phenylethylamine derivative of reserpine)
  ii. non-absorbable disaccharides (e.g. lactulose) which soften the stool by an osmotic effect and by lactic acid production from a bacterial fermenting effect
  iii. irritants, such as castor oil, which is hydrolysed in the small intestine releasing ricinoleic acid
- Bulking agents are hydrophilic and thus increase the water content of the stool.

Side-effects/complications

- Bloating and abdominal distension

- Diarrhoea if excessive amounts given

Notes

Surgical causes presenting as constipation such as bowel obstruction must be excluded. Other measures should be taken if possible to improve bowel function, e.g. reducing concurrent opiate dosage, starting enteral nutrition.

The agent of choice is lactulose.

Larger doses of lactulose are used in hepatic failure as the pH of the colonic contents is reduced; this lowers formation and absorption of ammonium ions and other nitrogenous products into the portal circulation. Proven benefit in patients has not been shown.

Anthraquinone glycosides (e.g. senna) and liquid paraffin are no longer recommended for routine use.

Drug dosages

Lactulose	15–50ml tds PO

See also:

Ovid: Oxford Handbook of Critical Care

Editors: Singer, Mervyn; Webb, Andrew R.
Title: *Oxford Handbook of Critical Care, 2nd Edition*

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Neurological Drugs

Opioid analgesics

Types

- Natural opiates: e.g. morphine, codeine
- Semisynthetic: e.g. diamorphine, dihydrocodeine
- Synthetic: e.g. pethidine, fentanyl, alfentanil, remifentanil

Uses

- Analgesia. Strong analgesics are extracts from opium or synthetic substances with similar properties. They are useful for continuous pain rather than sharp, intermittent pain.
- Sedation
- Mild vasodilatation in heart failure (diamorphine, morphine)
- Antidiarrhoeal (codeine)

Routes

- IV (morphine, diamorphine, papaveretum, pethidine, fentanyl, alfentanil, remifentanil)
- IM/SC (morphine, codeine, diamorphine, dihydrocodeine, pethidine)
- PO (morphine, codeine, diamorphine, dihydrocodeine, pethidine)

- Epidural (morphine, diamorphine, fentanyl, alfentanil)

Side-effects

- Respiratory depression
- Central nervous system depression
- Addiction (rare in the critically ill)
- Withdrawal syndrome (withdraw slowly)
- Stimulation of the vomiting centre
- Appetite loss
- Dry mouth
- Decreased gastric emptying and gut motility
- Histamine release and itching
- Increased muscular tone

Notes

Morphine is poorly absorbed from the gastrointestinal tract and is therefore usually administered parenterally. It is metabolised to morphine-6-glucuronide in the liver which is six times more potent than morphine and accumulates in renal failure.

Codeine is a weak analgesic but is favoured by some in head injury since it is less sedative than morphine.

Pethidine has local anaesthetic properties associated with cardiac depression and vasodilatation. It is metabolised to norpethidine which may lead to seizures on accumulation. Respiratory depression occurs despite maintenance of respiratory rate.

Fentanyl and alfentanil are good, short-acting analgesics with poor sedative quality. They cause severe respiratory depression and muscular rigidity. Remifentanil is ultra-short-acting and the patient may suffer from rebound pain if the infusion is stopped temporarily.

Drug dosages

Intravenous

	Bolus	Infusion
Morphine	0.1–0.2mg/kg	0.05–0.07mg/kg/h
Diamorphine	0.05–0.1mg/kg	0.03–0.06mg/kg/h
Pethidine	0.5mg/kg	0.1–0.3mg/kg/h
Fentanyl	5–7.5µg/kg	5–20µg/kg/h
Alfentanil	15–30µg/kg	20–120µg/kg/h
Remifentanil	1µg/kg	0.05–2µg/kg/min

Other routes

Morphine	10mg IM/SC 4-hrly	5–20mg PO 4-hrly
Codeine	30–60mg IM 4-hrly	30–60mg PO 4-hrly
Diamorphine	5mg IM/SC 4-hrly	5–10mg PO 4-hrly
Dihydrocodeine	50mg IM/SC 4–6-hrly	30mg PO 4–6-hrly
Pethidine	25–100mg IM/SC 4-hrly	50–150mg PO 4-hrly

Note that the above doses are a guide only and may need to be altered widely according to individual circumstances. The correct dose of an opiate analgesic is generally enough to ablate pain.

See also:
IPPV—failure to tolerate ventilation, p12; Non-opioid analgesics, p236; Sedatives, p238; Pain, p532; Post-operative intensive care, p534

Non-opioid analgesics

Types

- Non-steroidal anti-inflammatory drugs: e.g. aspirin, indomethacin, diclofenac
- Paracetamol
- Ketamine
- Nitrous oxide
- Local anaesthetics: e.g. lidocaine, bupivacaine

Uses

- Pain associated with inflammatory conditions (aspirin, indomethacin, diclofenac)
- Post-operative pain and musculoskeletal pain (aspirin, indomethacin, diclofenac, paracetamol, ketamine, nitrous oxide, lidocaine, bupivacaine)
- Opiate sparing effect (aspirin, indomethacin, diclofenac used with strong analgesics)
- Antipyretic (aspirin, paracetamol)

Routes

- IV (ketamine)
- IM (diclofenac)
- PO (aspirin, indomethacin, diclofenac, paracetamol)
- PR (aspirin, diclofenac, paracetamol)
- Local /regional (lidocaine, bupivacaine)
- Inhaled (nitrous oxide)

Side-effects

- Gastrointestinal bleeding (aspirin, indomethacin, diclofenac)
- Renal dysfunction (indomethacin, diclofenac if any hypovolaemia)
- Reduced platelet aggregation (aspirin, indomethacin, diclofenac)
- Reduced prothrombin formation (aspirin, indomethacin, diclofenac)
- Myocardial depression (lidocaine, bupivacaine)
- Hypertension and tachycardia (ketamine)
- Seizures (lidocaine, bupivacaine)

- Hallucinations and psychotic tendencies (ketamine—prevented by concurrent use of benzodiazepines or droperidol)

Notes

Paracetamol overdose can cause severe hepatic failure due to the effects of alkylating metabolites. Though normally removed by conjugation with glutathione, stores are rapidly depleted in overdose.

Non-steroidal anti-inflammatory agents should be generally avoided in patients with renal dysfunction, GI bleeding or coagulopathy.

Ketamine is a derivative of phencyclidine used as an intravenous anaesthetic agent. In subanaesthetic doses it is a powerful analgesic. It has several advantages over opiates in that it is associated with good airway maintenance, allows spontaneous respiration and provides cardiovascular stimulation. It is also a bronchodilator.

Nitrous oxide is a powerful, short acting analgesic used to cover short, painful procedures. It may be useful when delivered via an intermittent positive pressure breathing system as an adjunct to chest physiotherapy. Nitrous oxide should not be used in cases of undrained pneumothorax since it may diffuse into the pneumothorax resulting in tension.

Drug dosages

Aspirin	600mg PO/PR 4-hrly
Indomethacin	50–100mg PO/PR 12-hrly
Diclofenac	25–50mg PO 8-hrly, 100mg PR 12–24-hrly, 75mg IM 12-hrly
Ketorolac	10mg PO 4–6-hrly, 10–30mg IV, IM 4–6-hrly
Sulindac	200mg PO 12-hrly
Paracetamol	0.5–1g PO/PR 4–6-hrly
Ketamine	5–25µg/kg/min IV
Lidocaine	Maximum 200mg
Bupivicaine	Maximum 150mg*

*Local anaesthetic doses vary according to the area to be anaesthetised. Maximum doses may be increased if epinephrine is used locally.

See also:

Opioid analgesics, p234; Salicylate poisoning, p454; Rheumatic disorders, p492; Pyrexia (1), p518; Pyrexia (2), p520; Pain, p532; Post-operative intensive care, p534

Sedatives

Types

- Benzodiazepines: e.g. diazepam, midazolam, lorazepam
- Major tranquillisers: e.g. chlorpromazine, haloperidol
- Anaesthetic agents: e.g. propofol, isoflurane
- α_2 agonists e.g. clonidine, dexmedetomidine

Uses

- Sedation and anxiolysis

Routes

- IV (diazepam, midazolam, lorazepam, chlorpromazine, haloperidol, propofol, clonidine, dexmedetomidine)
- IM (diazepam, chlorpromazine, haloperidol)
- PO (diazepam, lorazepam, chlorpromazine, haloperidol, clonidine)
- Inhaled (isoflurane)

Side-effects

- Hypotension (diazepam, midazolam, chlorpromazine, haloperidol, propofol, clonidine, dexmedetomidine)
- Respiratory depression (diazepam, midazolam, chlorpromazine, haloperidol, propofol)
- Arrhythmias (chlorpromazine, haloperidol)
- Dry mouth (clonidine, dexmedetomidine)
- Extrapyramidal disorder (chlorpromazine, haloperidol)
- Fluoride toxicity (isoflurane)

Notes

Sedation is necessary for most ICU patients. While the appropriate use of sedative drugs can provide comfort, most have cardiovascular and respiratory side-effects. Objective assessment of the depth of sedation is necessary to ensure that comfort does not give way to excessively and dangerously deep levels of sedation. All sedatives are potentially cumulative so doses must be kept to a minimum.

Benzodiazepines have the advantage of being amnesic. Diazepam is mainly administered as an emulsion in intralipid as organic solvents are extremely irritant to veins. Midazolam is shorter acting than diazepam although 10% of patients are slow metabolisers. All benzodiazepines accumulate in renal failure; care must be taken to avoid excessive dosage by regular reassessment of need. Some patients suffer unpredictable severe respiratory depression with hypotension.

Propofol used in subanaesthetic doses is short-acting though effects are cumulative when infusions are prolonged or with coexisting hepatic or renal failure. It is given as an emulsion in 10% intralipid so large volumes may contribute significantly to calorie intake.

As chlorpromazine and haloperidol antagonise catecholamines, they may cause vasodilatation and hypotension. Dystonic reactions and arrhythmias are also occasionally seen.

α_2 antagonists also provide analgesia and are synergistic with opiates. Dexmedetomidine causes minimal respiratory depression and the patient is easily rousable. Bradycardia and hypotension may occur, especially with the loading dose.

Isoflurane is largely exhaled unchanged and is therefore short acting. Cumulative effects have been recorded with prolonged use, carrying the theoretical risk of fluoride toxicity. Exhaled isoflurane should be scavenged.

Drug dosages

	Bolus	Infusion
Diazepam	0.05–0.15mg/kg	Excessive half-life
Midazolam	50µg/kg	10–50µg/kg/h
Lorazepam	1mg PRN	
Propofol	0.5–2mg/kg	1–3mg/kg/h
Chlorpromazine	12.5–100mg	Excessive half-life
Clonidine		100–150µg/min
Dexmedetomidine		Loading infusion of 6.0µg/kg/h over 10min, followed by maintenance infusion of 0.2–0.7µg/kg/h.
Note that the above doses are a guide only and may need to be altered widely according to individual circumstances.		

Monitoring sedation

Frequent, objective reassessment of sedation depth with corresponding adjustment of infusion doses is necessary to avoid severe cardiovascular and respiratory depression. Simple sedation scores are available to aid assessment.

UCL Hospitals Sedation Score	
Agitated and restless	+3
Awake and uncomfortable	+2
Aware but calm	+1
Roused by voice, remains calm	0
Roused by movement	-1
Roused by painful or noxious stimuli	-2
Unrousable	-3
Natural sleep	A

Sedation doses are adjusted to achieve a score as close as possible to 0. Positive scores require increased sedation doses and negative scores require reduced sedation doses.

See also:

IPPV—failure to tolerate ventilation, p12; Opioid analgesics, p234; Agitation/confusion, p370; Sedative poisoning, p458; Post-operative intensive care, p534

Muscle relaxants

Types

- Depolarising: e.g. suxamethonium
- Non-depolarising: e.g. pancuronium, atracurium, vecuronium

Mode of action

- Suxamethonium is structurally related to acetylcholine and causes initial stimulation of muscular contraction seen clinically as fasciculation. During this process, the continued stimulation leads to desensitisation of the post-synaptic membrane of the neuromuscular junction with efflux of potassium ions. Subsequent flaccid paralysis is short acting (2–3min) and cannot be reversed (is actually potentiated) by anticholinesterase drugs. Prolonged effects are seen where there is congenital or acquired pseudocholinesterase deficiency.

- Non-depolarising muscle relaxants prevent acetylcholine from depolarising the post-synaptic membrane of the neuromuscular junction by competitive blockade. Reversal of paralysis is achieved by anticholinesterase drugs such as neostigmine. They have a slower onset and longer duration of action than the depolarising agents.

Uses

- To facilitate endotracheal intubation.
- To facilitate mechanical ventilation where optimal sedation does not prevent patient interference with the function of the ventilator.

Routes

- IV

Side-effects

- Hypertension (suxamethonium, pancuronium)
- Bradycardia (suxamethonium)

- Tachycardia (pancuronium)
- Hyperkalaemia (suxamethonium)

Notes

Modern intensive care practice and developments in ventilator technology have rendered the use of muscle relaxants less common. Furthermore, it is rarely necessary to fully paralyse muscles to facilitate mechanical ventilation.

Requirement for muscle relaxants should be reassessed frequently. Ideally, relaxants should be stopped intermittently to allow depth of sedation to be assessed. If mechanical ventilation proceeds smoothly when relaxants have been stopped they probably should not be restarted.

Suxamethonium is contraindicated in spinal neurological disease, hepatic disease and for 5–50 days after burns.

Atracurium is non-cumulative and popular for infusion. Non-enzymatic (Hoffman) degradation allows clearance independent of renal or hepatic function, although effects are prolonged in hypothermia.

Drug dosages

	Bolus	Infusion
Suxamethonium	50–100mg	2–5mg/min
Pancuronium	4mg	1–4mg/h
Atracurium	25–50mg	25–50mg/h
Vecuronium	5–7mg	Excessive half-life

See also:

IPPV—failure to tolerate ventilation, p12; Endotracheal intubation, p36; Sedatives, p238; Post-operative intensive care, p534

Anticonvulsants

Types

- Benzodiazepines: e.g. lorazepam, diazepam, clonazepam
- Phenytoin
- Carbamazepine
- Sodium valproate
- Magnesium sulphate
- Thiopental

Uses

- Control of status epilepticus
- Intermittent seizure control
- Myoclonic seizures (clonazepam, sodium valproate)

Routes

- IV (lorazepam, diazepam, clonazepam, phenytoin, sodium valproate, magnesium sulphate, thiopental)
- PO (diazepam, clonazepam, phenytoin, carbamazapine, sodium valproate)
- PR (diazepam)

Side-effects

- Sedation (benzodiazepines, thiopentone)
- Respiratory depression (benzodiazepines, thiopentone)

- Nausea and vomiting (phenytoin, sodium valproate)

- Ataxia (phenytoin, carbamazapine)

- Visual disturbance (phenytoin, carbamazapine)

- Hypotension (diazepam, thiopentone)

- Arrhythmias (phenytoin, carbamazapine)

- Pancreatitis (thiopentone)

- Hepatic failure (sodium valproate)

Notes

Common insults causing seizures include cerebral ischaemic damage, space occupying lesions, drugs or drug/alcohol withdrawal, metabolic encephalo-pathy (including hypoglycaemia), and neurosurgery. Anticonvulsants provide control of seizures but do not replace removal of the cause where this is possible.

Onset of seizure control may be delayed by up to 24h with phenytoin but a loading dose is usually given during the acute phase of seizures.

Magnesium sulphate is especially useful in eclamptic seizures (and in their prevention).

Phenytoin has a narrow therapeutic range and a non-linear relationship between dose and plasma levels. It is therefore essential to monitor plasma levels frequently. Enteral feeding should be stopped temporarily while oral phenytoin is administered. Intravenous use should only occur if the ECG is monitored continuously.

Carbamazepine has a wider therapeutic range than phenytoin and there is a linear relationship between dose and plasma levels. It is not, therefore, critical to monitor plasma levels frequently.

Plasma concentrations of sodium valproate are not related to effects so monitoring of plasma levels is not useful.

Intravenous drug dosages

	Bolus	Infusion
Lorazepam	4mg	
Diazepam	2.5mg repeated to 20mg	
Phenytoin	18mg/kg at <50mg/min	100mg 8hrly
Magnesium sulphate	20mmol over 10–20min	5–10mmol/h
Sodium valproate	400–800mg	
Clonazepam	1mg	1–2mg/h
Thiopental	1–3mg/kg	Lowest possible dose

Key trial

Treiman VA for the Veterans Affairs Status Epilepticus Cooperative Study Group. A comparison of four treatments for generalized convulsive status epilepticus. N Engl J Med 1998; 339:792–8

Magpie Trial Collaboration Group. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. Lancet 2002; 359:1877–90

Which anticonvulsant for women with eclampsia? Evidence from the Collaborative Eclampsia Trial. Lancet 1995; 345:1455–63

Neuroprotective agents

Types

- Diuretics: e.g. mannitol, furosemide (frusemide)

- Steroids: e.g. dexamethasone
- Calcium antagonists: e.g. nimodipine
- Barbiturates: e.g. thiopental

Uses

- Reduction of cerebral oedema (mannitol, furosemide, dexamethasone)
- Prevention of cerebral vasospasm (nimodipine)
- Reduction of cerebral metabolic rate (thiopental)

Routes

- IV

Notes

Cerebral protection requires generalised sedation and abolition of seizures to reduce cerebral metabolic rate, cerebral oedema and neuronal damage during ischaemia and reperfusion.

Mannitol reduces cerebral interstitial water by the osmotic load. The effect is transient and at its best where the blood–brain barrier is intact. Interstitial water is mainly reduced in normal areas of brain and this may accentuate cerebral shift. Repeated doses accumulate in the interstitium and may eventually increase oedema formation; mannitol should only be given 4–5 times in 48h. In addition to its osmotic effect, there is some evidence of cerebral vasoconstriction due to a reduction in blood viscosity and free radical scavenging.

The loop diuretic effect of furosemide encourages salt and water loss. There may also be a reduction of CSF chloride transport reducing the formation of CSF.

Dexamethasone reduces oedema around space occupying lesions such as tumours. Steroids are not currently considered useful in head injury or after a cerebrovascular accident but benefit has been shown if given early after spinal injury. Steroids encourage salt and water retention and must be withdrawn slowly to avoid rebound oedema.

Nimodipine is used to prevent cerebral vasospasm during recovery from cerebrovascular insults. As a calcium channel blocker it also prevents calcium ingress during neuronal injury. This calcium ingress is associated with cell death. It is commonly used in the management of subarachnoid haemorrhage for 5–14 days.

Thiopental reduces cerebral metabolism thus prolonging the time that the brain may sustain an ischaemic insult. However, it also reduces cerebral blood flow, although blood flow is redistributed preferentially to ischaemic areas. Thiopental acutely reduces intracranial pressure and this is probably the main cerebroprotective effect. Seizure control is a further benefit. Despite these effects, barbiturate coma has not been shown to improve outcome in cerebral insults of various causes.

Drug dosages

	Bolus	Infusion
Mannitol	20–40g 6-hrly	
Furosemide		1–5mg/h
Dexamethasone	4mg 6-hrly	
Nimodipine		0.5–2.0mg/h
Thiopental	1–3mg/kg	Lowest possible dose

Key trials

Allen GS et al. Cerebral arterial spasm—a controlled trial of nimodipine in patients with subarachnoid hemorrhage. N Engl J Med 1983; 308:619–24

Bracken MB, et al. Administration of methylprednisolone for 24 or 48 hours or tirilazad mesylate for 48 hours in the treatment of acute spinal cord injury. Results of the Third National Acute Spinal Cord Injury Randomized Controlled Trial. National Acute Spinal Cord Injury Study. JAMA 1997; 277:1597–604

See also:

Ovid: Oxford Handbook of Critical Care

Editors: **Singer, Mervyn; Webb, Andrew R.**
Title: ***Oxford Handbook of Critical Care, 2nd Edition***

Haematological Drugs

Anticoagulants

Types

- Heparin
- Low molecular weight (LMW) heparin: e.g. dalteparin, enoxiparin
- Anticoagulant prostanoids: e.g. epoprostenol, alprostadil
- Sodium citrate
- Warfarin
- Activated Protein C

Modes of action

- Heparin potentiates naturally occurring AT-III, reduces the adhesionof platelets to injured arterial walls, binds to platelets and promotes *in vitro* aggregation.
- LMW heparin appears to specifically influence factor Xa activity; its simpler pharmacokinetics allow for a smaller (two thirds) dose to be administered to the same effect.
- The effects of the prostanoids depend on the balance between TXA_2 and PGI_2.
- Sodium citrate chelates ionised calcium.
- Warfarin produces a controlled deficiency of vitamin K dependent coagulation factors (II, VII, IX and X).
- Activated Protein C is the activated form of the endogenous anticoagulant, Protein C

Uses

- Maintenance of an extracorporeal circulation
- Prevention or treatment of thromboembolism
- Severe sepsis (activated Protein C)

Routes

- IV (heparins, anticoagulant prostanoids, sodium citrate, activated Protein C, AT-III)
- SC (heparins)
- PO (warfarin)

Side-effects

- Bleeding
- Hypotension (anticoagulant prostanoids)
- Heparin induced thrombocytopenia
- Hypocalcaemia and hypernatraemia (sodium citrate)

Notes

Alprostadil has similar effects to epoprostanil but is less potent. As it is metabolised in the lungs, systemic vasodilatation effects are usually minimal. This may be an important advantage in the shocked patient. Major uses in

intensive care are for anticoagulation of filter circuits, digital vasculitis/ischaemia and pulmonary hypertension.

For extracorporeal use citrate has advantages over heparin in that it has no known antiplatelet activity, is readily filtered by a haemofilter (reducing systemic anticoagulation), and is overwhelmed and neutralised when returned to central venous blood.

Warfarin is given orally and needs 48–72h to develop its effect. It can be reversed by fresh frozen plasma or low doses (1mg) of vitamin K.

Activated Protein C has anti-inflammatory and pro-fibrinolytic properties in addition to its anticoagulant actions.

Drug dosages

Heparin
Dose requirement is variable to produce an APTT of 1.5–3 times control. This usually requires 500–2000IU/h with an initial loading dose of 3000–5000IU.

Low molecular weight heparin
For deep vein thrombosis prophylaxis give 2500IU SC 12-hrly. For anticoagulation of an extracorporeal circuit a bolus of 35IU/kg is given IV followed by an infusion of 13IU/kg. The dose is adjusted to maintain anti-factor Xa activity at 0.5–1IU/ml (or 0.2–0.4IU/ml if there is a high risk of haemorrhage).

For pulmonary embolism give 200IU/kg SC daily (or 100IU/kg bd if at risk of bleeding)

Anticoagulant prostaglandins
Usual range of 2.5–10ng/kg/min. If used for an extracorporeal circulation the infusion should be started 30min prior to commencement.

Sodium citrate
Infused at 5mmol per litre of extracorporeal blood flow.

Warfarin
Start at 10mg/day orally for 2 days then 1–6mg/day according to INR. For DVT prophylaxis, pulmonary embolus, mitral stenosis, atrial fibrillation and tissue valve replacements the INR should be maintained between2 and 3. For recurrent DVT or pulmonary embolus and mechanical valve replacements the INR should be kept between 3 and 4.5.

Activated Protein C (Drotrecogin α activated)
For sepsis, an infusion of 24 μg/kg/h is given for 96h.

See also:
Extracorporeal respiratory support, p34; Haemo(dia)filtration (2), p64; Plasma exchange, p68; Coagulation monitoring, p156; Thrombolytics, p250; Pulmonary embolus, p308; Acute coronary syndrome (1), p320; Acute coronary syndrome (2), p322; Clotting disorders, p398; Hyperosmolar diabetic emergencies, p444; Sepsis and septic shock—treatment, p248; Post-operative intensive care, p534

Thrombolytics

Types

- Alteplase (rt-PA)
- Streptokinase
- Urokinase

Modes of action
Activate plasminogen to form plasmin which degrades fibrin

Uses

- Life threatening venous thrombosis
- Life threatening pulmonary embolus
- Acute myocardial infarction
- To unblock indwelling vascular access catheters

Routes

- IV

Side-effects

- Bleeding, particularly from invasive procedures
- Hypotension and arrhythmias
- Embolisation from pre-existing clot as it is broken down
- Anaphylactoid reactions (anistreplase, streptokinase, urokinase)

Contraindications (absolute)

- Cerebrovascular accident in last 2 months
- Active bleeding in last 10 days
- Pregnancy
- Recent peptic ulceration
- Recent surgery

Contraindications (relative)

- Systolic BP >200mmHg
- Aortic dissection
- Proliferative diabetic retinopathy

Notes

In acute myocardial infarction they are of most value when used within 12h of the onset. They may require adjuvant therapy (e.g. aspirin with streptokinase or heparin with rt-PA) to maximise the effect in acute myocardial infarction.

rt-PA is said to be clot selective and is therefore useful where a need for invasive procedures has been identified.

Anaphylactoid reactions to streptokinase are not uncommon, particularly in those who have had streptococcal infections, and patients should not be exposed twice between 5 days and 1 year of receiving the last dose.

Drug dosages

Alteplase (rt-PA)	The dose schedule for acute myocardial infarction is 10mgin 1–2min, 50mg in 1h and 40mg over 2h intravenously.
Anistreplase	Single intravenous injection of 30U over 4–5min.
Streptokinase	In acute myocardial infarction (1.5mu over 60min).In severe venous thrombosis (250,000U over 30min followed by 100,000U/h for 24–72h).
Urokinase	For unblocking indwelling vascular catheters 5000–37,500IU are instilled.
	For thromboembolic disease 4400IU/kg is given over 10min followed by 4400IU/kg/h for 12–24h.

See also:

Blood products

Types

- Plasma: e.g. fresh frozen plasma
- Platelets
- Concentrates of coagulation factors: e.g. cryoprecipitate, factor VIII concentrate, factor IX complex

Uses

- Vitamin K deficiency (fresh frozen plasma, factor IX complex)
- Haemophilia (cryoprecipitate)
- von Willebrand's disease (cryoprecipitate)
- Fibrinogen deficiency (cryoprecipitate)
- Christmas disease (factor IX complex)

Routes

- IV

Notes

A unit (150ml) of fresh frozen plasma is usually collected from one donor and contains all coagulation factors including 200 units factor VIII, 200 units factor IX and 400mg fibrinogen. Fresh frozen plasma is stored at -30°C and should be infused within 2h once defrosted.

Platelet concentrates are viable for 3 days when stored at room temperature. If they are refrigerated viability decreases. They must be infused quickly via a short giving set with no filter. Indications for platelet concentrates include platelet count $<10 \times 10^9$, or $<50 \times 10^9$ with spontaneous bleeding, or to cover invasive procedures and spontaneous bleeding with platelet dysfunction. They are less useful in conditions associated with immune platelet destruction (e.g. ITP).

A 15ml vial of cryoprecipitate contains 100 units factor VIII, 250mg fibrinogen, factor XIII and von Willebrand factor and is stored at -30°. In haemophilia, cryoprecipitate is given to achieve a factor VIII level >30% of normal.

Factor VIII concentrate contains 300 units factor VIII per vial. In severe haemorrhage due to haemophilia 10–15 units/kg are given 12-hrly.

Factor IX complex is rich in factors II, IX and X. It is formed from pooled plasma so fresh frozen plasma is preferred.

See also:

Coagulants and antifibrinolytics

Types

- Vitamin K
- Protamine
- Tranexamic acid
- Activated factor VII (F VIIa)

Uses

- To reverse a prolonged prothrombin time, e.g. malabsorption, oral anticoagulant therapy, β lactam antibiotics or critical illness (vitamin K)
- To reverse the effects of heparin (protamine)
- Bleeding from raw surfaces, e.g. prostatectomy, dental extraction (tranexamic acid)
- Bleeding from thrombolytics (tranexamic acid)
- Bleeding from major trauma or haemophilia (F VIIa)

Routes

- IV (vitamin K, protamine, tranexamic acid, F VIIa)
- PO (vitamin K, tranexamic acid)

Notes

The effects of vitamin K are prolonged so it should be avoided where patients are dependent on oral anticoagulant therapy. A dose of 10mg is given orally or by slow intravenous injection daily. In life threatening haemorrhage

5–10mg is given by slow intravenous injection with other coagulation factor concentrates. If INR >7 or in less severe haemorrhage 0.5–2mg may be given by slow intravenous injection with minimum lasting effect on oral anticoagulant therapy.

Protamine has an anticoagulant effect of its own in high doses. Protamine 1mg neutralises 100IU unfractionated heparin if given within 15min. Less is required if given later since heparin is excreted rapidly. Protamine should be given by slow intravenous injection according to the APTT. Total dose should not exceed 50mg. Protamine injection may cause severe hypotension

Tranexamic acid has an antifibrinolytic effect by antagonising plasminogen. The usual dose is 1–1.5g 6–12-hrly orally or by slow intravenous injection.

Recombinant factor VIIa is licensed for use in haemophilia but a number of case series in major trauma, orthopaedic and cardiac surgery report benefit in severe, intractable bleeding that had not responded to standard measures. The dose is 4500IU/kg over 2–5min, followed by 3000–6000IU/kg depending on the severity of bleeding.

See also:

Aprotinin
The role of serine protease inhibitors in coagulation and anticoagulation is complicated due to their effects at various points in the coagulation pathway. Aprotinin is a naturally occurring, non-specific serine protease inhibitor with an elimination half-life of about 2h. Prevention of systemic bleeding with aprotinin does not promote coagulation within the extracorporeal circulation and may even contribute to the maintenance of extracorporeal anticoagulation.

Modes of action
The effects of aprotinin on the coagulation cascade are dependent on the circulating plasma concentrations (expressed as kallikrein inactivation units—kIU/ml) since the affinity of aprotinin for plasmin is significantly greater than that for plasma kallikrein. At a plasma level of 125kIU/ml aprotinin inhibits fibrinolysis and complement activation. Inhibition of plasma kallikrein requires higher doses to provide plasma levels of 250–500kIU/ml.

- Plasma kallikrein inhibition—reduces blood coagulation mediated via contact with anionic surfaces and, in the critically ill patient, improves circulatory stability via reduced kinin activation.
- Prevention of inappropriate platelet activation—neutrophil activation (complement or kallikrein mediated) causes a secondary activation of platelets. Important in this platelet–neutrophil interaction is the release of Cathepsin G by neutrophil degranulation. It has been demonstrated recently that aprotinin can significantly inhibit the platelet activation due to purified Cathepsin G, this mechanism forming a direct inhibition of inappropriate neutrophil mediated platelet activation.

Uses
- The main role of aprotinin in the management of the extracorporeal circulation has been to prevent bleeding associated with heparinisation. High dose aprotinin given during cardiopulmonary bypass procedures has been shown to reduce post-operative blood loss dramatically.

Drug dosages

Aprotinin—loading dose of 2×10^{6}kIU followed by 500,000kIU/h

See also:

Miscellaneous Drugs

Antimicrobials

Types

- Penicillins: e.g. benzylpenicillin, flucloxacillin, piperacillin, ampicillin
- Cephalosporins: e.g. cefotaxime, ceftazidime, cefuroxime
- Carbapenems: e.g. imipenem, meropenem
- Aminoglycosides: e.g. gentamicin, amikacin, tobramycin
- Quinolones: e.g. ciprofloxacin
- Glycopeptides: e.g. teicoplanin, vancomycin
- Macrolides: e.g. erythromycin, clarithromycin
- Other antibacterials:. e.g. clindamycin, metronidazole, linezolid, co-trimoxazole, rifampicin
- Antifungals: e.g. amphotericin, flucytosine, fluconazole, caspofungin, voriconazole, itraconazole
- Antivirals: e.g. aciclovir, ganciclovir

Uses

- Treatment of infection.
- Prophylaxis against infection, e.g. peri-operatively
- Local choice of antimicrobial varies. However, as a guide, the following choices are common:

  Pneumonia (hospital-acquired Gram negative)—ceftazidime, ciprofloxacin, meropenem or piperacillin/tazobactam (piptazobactam)

  Pneumonia (community-acquired)—cefuroxime + clarithromycin

  Systemic sepsis—cefuroxime ± gentamicin (+ metronidazole if anaerobes likely)

Routes
Generally IV in critically ill patients.

Side-effects

- Hypersensitivity reactions (all)
- Seizures (high dose penicillins, high dose metronidazole, ciprofloxacin)
- Gastrointestinal disturbance (cephalosporins, erythromycin, clindamycin, teicoplanin, vancomycin, co-trimoxazole, rifampicin, metronidazole, ciprofloxacin, amphotericin, flucytosine)
- Vestibular damage (aminoglycosides)
- Renal failure (aminoglycosides, teicoplanin, vancomycin, ciprofloxacin, rifampicin, amphotericin, aciclovir)
- Erythema multiforme (co-trimoxazole)
- Leucopenia (co-trimoxazole, metronidazole, teicoplanin, ciprofloxacin, flucytosine, aciclovir)
- Thrombocytopenia (linezolid)
- Peripheral neuropathy (metronidazole)

Notes
Antimicrobials should be chosen according to microbial sensitivities, usually based on advice from the microbiology laboratory.

Appropriate empiric therapy for serious infections should be determined by likely organisms, taking into account known community and hospital infection and resistance patterns.

Up to 10% of penicillin-allergic patients are also cephalosporin-allergic.

Drug dosages (intravenous)

Benzylpenicillin	1.2g 6-hrly (2-hrly for pneumococcal pneumonia)
Flucloxacillin	500mg–2g 6-hrly
Ampicillin	500mg–1g 6-hrly
Piptazobactam	4.5g 6–8-hrly
Cefotaxime	1–4g 8-hrly
Ceftazidime	2g 8-hrly
Ceftriaxone	1–4g daily
Cefuroxime	750mg–1.5g 8-hrly
Gentamicin	1.5mg/kg stat then by levels (usually 80mg 8-hrly)
Amikacin	7.5mg/kg stat then by levels (usually 500mg 12-hrly)
Tobramycin	5mg/kg stat then by levels (usually 100mg 8-hrly)
Erythromycin	500mg–1g 6–12-hrly
Metronidazole	500mg 8-hrly or 1g 12-hrly PR
Clindamycin	300–600mg 6-hrly
Ciprofloxacin	200–400mg 12-hrly
Co-trimoxazole	960mg 12-hrly in *Pneumocystis carinii* pneumonia
Imipenem	1–2g 6–8-hrly
Meropenem	500mg–1g 8-hrly
Rifampicin	600mg daily
Teicoplanin	400mg 12-hrly for 3 doses then 400mg daily
Vancomycin	500mg 6-hrly (monitor levels)
Linezolid	600mg 12-hrly
Chloramphenicol	1–2g 6-hrly
Amphotericin	250µg–1mg/kg daily
Flucytosine	25–50mg/kg 6-hrly
Fluconazole	200–400mg daily
Caspofungin	70mg stat then 50–70mg daily
Voriconazole	400mg 12-hrly on first day then 200–300mg 12-hrly
Itraconazole	200mg 12-hrly for 2 days then 200mg daily

Common choices for specific organisms

Staph. aureus	flucloxacillin
Methicillin-resistant Staph. aureus	teicoplanin, vancomycin, linezolid
Strep. pneumoniae	cefuroxime, benzylpenicillin
N. meningitidis	ceftriaxone, cefotaxime, benzylpenicillin
H. influenzae	cefuroxime, cefotaxime
E. coli	ampicillin, ceftazidime, ciprofloxacin, gentamicin, ciprofloxacin, gentamicin, imipenem, meropenem
Klebsiella spp.	ceftazidime, ciprofloxacin, gentamicin, imipenem, meropenem
Ps. aeruginosa	ceftazidime, ciprofloxacin, gentamicin, imipenem, meropenem, piptazobactam

Steroids

Uses

- Anti-inflammatory—steroids are often given in high dose for their anti-inflammatory effect, e.g. asthma, allergic and anaphylactoid reactions, vasculitic disorders, rheumatoid arthritis, inflammatory bowel disease, neoplasm-related cerebral oedema, the fibro-proliferative phase of ARDS, pneumococcal meningitis, pneumocystis pneumonia, laryngeal oedema (e.g. after repeated intubation) and after spinal cord injury. Benefit is unproved as yet in cerebral oedema following head injury or cardiorespiratory arrest, and may be harmful in cerebral malaria and sepsis (at high dose).

- A multicentre trial has shown improved outcomes with 'low dose' hydrocortisone (50mg qds for one week) in septic shock patients with depressed adrenal function (subnormal plasma cortisol response to ACTH, often despite 'normal' or raised plasma levels). Some patients with hypotension not responding to catecholamines will improve with corticosteroid therapy.

- Replacement therapy is needed for patients with Addison's disease and after adrenalectomy or pituitary surgery. In the longer term, fludrocortisone is usually required in addition for its mineralocorticoid sodium-retaining effect. Higher replacement doses are needed in chronic steroid takers (i.e. >2 weeks within the last year) undergoing a stress, e.g. surgery, infection.

- Immunosuppressive—after organ transplantation

Side-effects/complications

- Sodium and water retention (especially with mineralocorticoids)
- Hypoadrenal crisis if stopped abruptly after prolonged treatment
- Immunosuppressive—possibly increased infection risk *(q.v.)*
- Neutrophilia
- Impaired glucose tolerance/diabetes mellitus
- Hypokalaemic alkalosis
- Osteoporosis, proximal myopathy (long-term use)
- Increased susceptibility to peptic ulcer disease and GI bleeding

Notes

The perceived heightened risk of systemic infection appears exaggerated. Chronic steroid users generally appear no more affected than the general population; studies in ARDS and sepsis revealed no greater incidence of infection post-steroid administration. Oral fungal infection is relatively common with inhaled steroids but systemic and pulmonary fungal infection is predominantly seen in the severely immunocompromised (e.g. AIDS, post-chemotherapy) and not those taking high-dose steroids alone.

The choice of corticosteroid for short-term anti-inflammatory effect is probably irrelevant provided the dose is sufficient. Chronic hydrocortisone should be avoided for anti-inflammatory use because of its mineralocorticoid effect but is appropriate for adrenal replacement.

Prednisone and cortisone are inactive until metabolised by the liver to prednisolone and hydrocortisone respectively. Glucocorticoids antagonise the effects of anticholinesterase drugs.

Steroids are probably not likely to cause critical illness myopathy though this remains a contentious issue.

Relative potency and activity

Drug	Glucocorticoid activity	Mineralocorticoid activity	Equivalent anti-inflammatory dose (mg)
Cortisone	+ +	+ +	25
Dexamethasone	+ + + +	—	0.75
Hydrocortisone	+ +	+ +	20
Methylprednisolone	+ + +	+	4
Prednisolone	+ + +	+	5
Prednisone	+ + +	+	5
Fludrocortisone	+	+ + + +	—

Drug dosages

Drug	Replacement dose	Anti-inflammatory dose
Dexamethasone	—	4–20mg tds IV
Hydrocortisone	20–30mg daily	100–200mg qds IV
Methylprednisolone	—	500mg–1g IV daily
Prednisolone	2.5–15mg mane	40–60mg od PO
Fludrocortisone	0.05–0.3mg daily	—

Weaning

Acute use (<3–4 days)	can stop immediately
Short-term use ≥3–4 days)	wean over 2–5 days
Medium-term use (weeks)	wean over 1–2 weeks
Long-term use (months/years)	wean slowly (months to years)

Key papers

Annane D, Sebille V, Charpentier C et al. Effect of treatment with low doses of hydrocortisone and fludrocortisone on mortality in patients with septic shock. JAMA 2002; 288:862–71

Bracken MB, et al. Administration of methylprednisolone for 24 or 48 hours or tirilazad mesylate for 48 hours in the treatment of acute spinal cord injury. Results of the Third National Acute Spinal Cord Injury Randomized Controlled Trial. National Acute Spinal Cord Injury Study. JAMA 1997; 277:1597–604

Prasad K, Garner P. Steroids for treating cerebral malaria. Cochrane Database Syst Rev 2000; (2):CD000972. Review.

de Gans J, van de Beek D; European Dexamethasone in Adulthood Bacterial Meningitis Study Investigators. Dexamethasone in adults with bacterial meningitis. N Engl J Med 2002; 347:1549–56

van de Beek D, et al. Corticosteroids in acute bacterial meningitis. Cochrane Database Syst Rev 2003; (3):CD004305. Review.

Prostaglandins

Types

- Epoprostenol (prostacyclin, PGI_2)
- Alprostadil (PGE_1)

Modes of action

- Stimulate adenyl cyclase thus increasing platelet cAMP concentration; this inhibits phospholipase and cycloxygenase and thus reduces platelet aggregation (epoprostenol is the most potent inhibitor known)
- Reduces platelet procoagulant activity and release of heparin neutralising factor
- May have a fibrinolytic effect
- Pulmonary and systemic vasodilator by relaxation of vascular smooth muscle

Uses

- Anticoagulation, particularly for extracorporeal circuits, either as a substitute or in addition to heparin
- Pulmonary hypertension
- Microvascular hypoperfusion (including digital vasculitis)
- Haemolytic uraemic syndrome
- Acute respiratory failure (by inhalation)

Side-effects/complications

- Hypotension
- Bleeding (particularly at cannula sites)
- Flushing, headache

Notes

Epoprostenol is active on both pulmonary and systemic circulations.

Although alprostadil is claimed to be metabolised in the lung and have only pulmonary vasodilating effects, falls in systemic blood pressure are not uncommonly seen, especially if metabolism is incomplete.

Avoid extravasation into peripheral tissues as solution has high pH.

Effects last up to 30min following discontinuation of the drug.

Prostaglandins may potentiate the effect of heparin.

Recent studies have shown improvement in gas exchange by selective pulmonary vasodilatation following inhalation of epoprostenol at doses of 10–15ng/kg/min. The efficacy appears similar to that of nitric oxide inhalation but is not as rapid.

Drug dosages

Epoprostenol	2–20ng/kg/min
Alprostadil	2–20ng/kg/min

See also:

Novel therapies in sepsis

Greater understanding of the pathophysiology of sepsis has stimulated the development and investigation of agents that modulate different components of the inflammatory response. These drugs have been targeted at triggers (e.g. endotoxin), cytokines (e.g. tumour necrosis factor, interleukin (IL)-1), and effector cells and their products (e.g. neutrophils, free oxygen radicals, nitric oxide) or aim to boost a general anti-inflammatory response (e.g. steroids). An increasing area of research is in replacement or augmentation of endogenous anti-inflammatory systems, e.g. activated Protein C, antithrombin-III, IL-10, as there is an increasing realisation of the degree of disruption and imbalance between pro- and anti-inflammatory substances.

Unfortunately, due to deficiencies in trial design and size, choice of appropriate patient, timing of drug administration, dosage, and lack of standardisation of concurrent therapies, only two agents ('low dose' hydrocortisone and activated Protein C) have been shown to produce outcome benefit in reasonably sized multicentre trials. For many other products, promising results from *post-hoc* subgroup analysis and from tightly controlled small patient studies have not been reproduced. Concern over cost has highlighted the potential budgetary implications of any successful therapy though, in terms of life years, the cost–benefit will be relatively cheap.

Uses

- Sepsis
- Multiple-organ dysfunction

Activated Protein C

Activated Protein C has anti-inflammatory, anticoagulant and pro-fibrinolytic properties. Its beneficial effects in sepsis are most likely to be related to its anti-inflammatory properties. A large prospective randomised controlled trial demonstrated outcome benefit for patients with severe sepsis treated within 48h of presentation with a 96h infusion of 24μg/kg/h aPC. Most benefit was seen in those with ≥2 organ dysfunctions. The major side effect was bleeding so caution should be exercised in those at high risk of potentially catastrophic bleeding, e.g. concurrent coagulopathy, or a recent history of surgery, major trauma, head injury and/or peptic ulcer disease.

Corticosteroids

Large randomised multicentre studies of high dose methyl prednisolone showed either no benefit or a trend to harm. However, subsequent studies with lower doses of corticosteroids (e.g. 50mg qds hydrocortisone) revealed earlier resolution of shock and improved survival in those patients with an impaired (<250nmol/l [9μg/dl]) rise in plasma cortisol to a synthetic ACTH challenge.

Examples of drugs investigated in multicentre studies

- Corticosteroids (methylprednisolone, hydrocortisone)
- Polyclonal immunoglobulin
- Anti-endotoxin antibody (HA-1A, E5)
- Antitumour necrosis factor antibody
- Tumour necrosis factor soluble receptor antibody
- Interleukin-1 receptor antagonist
- Platelet activating factor antagonists, PAF-ase
- Bradykinin antagonists
- Naloxone

- Ibuprofen

- *N*-acetylcysteine, procysteine

- L-*N*-mono-methyl-arginine (L-NMMA)

- Antithrombin III

- Tissue factor pathway inhibitor

- Activated Protein C

Key trials

Bernard GR, for the PROWESS study group. Efficacy and safety of recombinant human activated protein C for severe sepsis. N Engl J Med 344:699–709

Annane D, et al. Effect of treatment with low doses of hydrocortisone and fludrocortisone on mortality in patients with septic shock. JAMA 2002; 288:862–71

See also:

Sepsis and septic shock—treatment, p486

Resuscitation

Basic resuscitation

In any severe cardiorespiratory disturbance the order of priority should be to secure the airway, maintain respiration (i.e. manual ventilation if necessary), restore the circulation (with external cardiac massage if necessary) and consider mechanical ventilation. Initial assessment of the patient should include patency of the airway, palpation of the pulses, measurement of blood pressure, presumptive diagnosis and consideration of treatment of the cause.

Airway protection

The airway should be opened by lifting the jaw forward and tilting the forehead. The mouth and pharynx should be cleared by suction and loose fitting dentures removed. If necessary an oropharyngeal (Guedel) airway may be inserted.

Manual ventilation

Once the airway is protected the patient who is not breathing requires manual ventilation with a self-inflating bag and mask (Ambu bag). Oxygen should be delivered in maximum concentration (FIO_2 1.0 for manual ventilation, FIO_2 0.6–1.0 for spontaneously breathing patients). If the patient breathes inadequately (poor arterial saturation, hypercapnia, rapid shallow breathing) ventilatory support should continue.

Circulation

If pulses are not palpable or are weak or if the patient has a severe bradycardia external cardiac massage is required and treatment should continue as for a cardiac arrest. Hypotension should be treated initially with a fluid challenge although life-threatening hypotension may require blind treatment with epinephrine 0.05–0.2mg increments at 1–2min intervals intravenously until a satisfactory blood pressure is restored. Such treatment should not be prolonged without circulatory monitoring to ensure adequacy of cardiac output as well as correction of hypotension.

Venous access

Venous access must be secured early during basic resuscitation. Large-bore cannulae are necessary, e.g. 14G. In cases of haemorrhage two cannulae are required. Small peripheral veins should be avoided; forearm flexure veins are appropriate if nowhere else is available. In very difficult patients a Seldinger approach to the femoral vein or a central vein may be appropriate. The latter has the advantage of providing central venous monitoring.

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See also:

Oxygen therapy, p2; Ventilatory support—indications, p4; Endotracheal intubation, p36; Central venous catheter—insertion, p116; Colloids, p180; Inotropes, p196; Vasopressors, p200; Fluid challenge, p274; Hypotension, p312

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Cardiac arrest

As with basic resuscitation the order of priority is airway, breathing and circulation followed by drug treatment. If the cardiac arrest is witnessed a precordial thump may revert ventricular tachycardia or ventricular fibrillation. Initial management of the airway and respiration is as for basic resuscitation. When intubation is attempted it should be effected after adequate pre- oxygenation and quickly to avoid hypoxaemia. If intubation is difficult maintain manual ventilation with an Ambu bag, mask and 100% oxygen.

Cardiac massage

External cardiac massage provides minimal circulatory support during cardiac arrest. A compression rate of 80–100/min is likely to provide the optimum blood flow during cardiac massage with a manual breath from an assistant for every 5 compressions. Avoid massage during manual inspiration if the patient is not intubated (to avoid gastric dilatation); otherwise cardiac massage is more effective if not synchronised to respiration.

Defibrillation

Defibrillation should be performed urgently if VT or VF cannot be excluded. It is important to restart cardiac massage immediately after defibrillation without waiting for the ECG to recover. Cerebral damage continues while there is no blood flow.

Drugs

Few drugs are necessary for first line cardiac arrest management. Drugs should be given via a large vein since vasoconstriction and poor flow create delay in injections given via small peripheral veins reaching the central circulation. Access should be secured early during the resuscitation; if venous access cannot be secured double or triple doses of drugs may be given via the endotracheal tube.

Epinephrine

The α constrictor effects predominate during cardiac arrest, helping to maintain diastolic blood pressure and thus coronary and cerebral perfusion. Epinephrine should be given irrespective of rhythm at 1mg (10ml of 1:10,000 solution) every 10 CPR sequences.

Vasopressin

A recent randomized controlled trial comparing vasopressin and epinephrine showed improved outcomes with vasopressin for patients in asystole.

Atropine

A single 3mg dose is given early in asystole.

Calcium chloride

Used in electromechanical dissociation if there is hyperkalaemia, hypocalcaemia or calcium antagonist use. A dose of 10ml of a 10% solution is usual. The main disadvantage of calcium is the reduction of reperfusion of ischaemic brain and promotion of cytosolic calcium accumulation during cell death.

Bicarbonate

Only used if resuscitation is prolonged to correct temporarily a potentially lethal pH. A dose of 50ml of 8.4% solution is given. The main disadvantage is that intracellular and respiratory acidosis are exacerbated unless ventilation is increased and the cause of the metabolic acidosis is not corrected.

Key trial

Wenzel V for the European Resuscitation Council Vasopressor during CPR study. A comparison of vasopressin and epinephrine for out-of- hospital cardiopulmonary resuscitation. N Engl J Med 2004; 350:105–13

Fluid challenge

Hypovolaemia must be treated urgently to avoid the serious complication of organ failure. An adequate circulating volume must be provided before considering other methods of circulatory support. Clinical signs of hypovolaemia (reduced skin turgor, low CVP, oliguria, tachycardia and hypotension) are late indicators. Lifting the legs of a supine patient and watching for an improvement in the circulation is a useful indicator of hypovolaemia. A high index of suspicion must be maintained; a normal heart rate, blood pressure and CVP do not exclude hypovolaemia and the CVP is particularly unreliable in pulmonary vascular disease, right ventricular disease, isolated left ventricular failure and valvular heart disease. The absolute CVP or PAWP are also difficult to interpret since peripheral venoconstriction may maintain these filling pressures despite hypovolaemia; indeed, they may fall in response to fluid. The response to a fluid challenge is the safest method of assessment.

Choice of fluid

The aim of a fluid challenge is to produce a significant (200ml) and rapid increase in plasma volume. Colloid fluids

are ideal; a gelatin solution is recommended for short term plasma volume expansion in simple hypovolaemia, and hydroxyethyl starch where there is a probability of capillary leak. Packed red cells have a high haematocrit and do not adequately expand the plasma volume. Crystalloid fluids are rapidly lost from the circulation and do not give a reliable increase in plasma volume.

Assessing the response to a fluid challenge

Ideally, the response of CVP, or stroke volume and PAWP, should be monitored during a fluid challenge. Fluid challenges should be repeated while the response suggests continuing hypovolaemia. However, if such monitoring is not available it is reasonable to assess the clinical response to up to two fluid challenges (200ml each).

CVP response

The change in CVP after a 200ml fluid challenge depends on the starting blood volume (see figure). A 3mmHg rise in CVP represents a significant increase and is probably indicative of an adequate circulating volume. However, a positive response may sometimes occur in the vasoconstricted patient with a lower blood volume. It is important to assess the clinical response in addition; if inadequate, it is appropriate to monitor stroke volume and PAWP before further fluid challenges or considering further circulatory support.

Stroke volume and PAWP response

In the inadequately filled left ventricle a fluid challenge will increase the stroke volume. Failure to increase the stroke volume with a fluid challenge may represent an inadequate challenge, particularly if the PAWP fails to rise significantly (3mmHg). This indicates that cardiac filling was inadequate and the fluid challenge should be repeated. Such a response may also be seen in right heart failure, pericardial tamponade and mitral stenosis. It is important to monitor stroke volume rather than cardiac output during a fluid challenge. If the heart rate falls appropriately in response to a fluid challenge the cardiac output may not increase despite an increase in stroke volume.

CVP and stroke volume response to fluid challenge

CVP/PAWP

>3mmHg

3mmHg

<3mmHg

Blood volume

Stroke volume

Blood volume

— Under filled
— Well filled
— Over filled

Figure. No Caption Available.

See also:

Respiratory Disorders

Dyspnoea

Defined as difficulty in breathing. The respiratory rate may be increased or decreased, though the respiratory effort is usually increased with the use of accessory muscles. The patient may show signs of progressive fatigue and

impaired gas exchange.

Commoner ICU causes

Respiratory	respiratory failure
Circulatory	heart failure, hypoperfusion, pulmonary embolus, severe anaemia
Metabolic	acidosis
Central	stimulants, e.g. aspirin
Anaphylactic	upper airway obstruction, bronchospasm
Psychiatric	hysterical

Principles of management

1. O_2 therapy to maintain SaO_2 (ideally >90–95%)
2. Correct abnormality where possible
3. Support therapy until recovery
   - mechanical, e.g. positive pressure ventilation, CPAP
   - pharmacological treatment, e.g. bronchodilators, vasodilators
4. Relieve anxiety

A psychiatric cause of dyspnoea is only made after exclusion of other treatable causes.

Dual co-existing pathologies should be considered, e.g. chest infection and hypovolaemia.

See also:

Airway obstruction

Causes

- In the lumen, e.g. foreign body, blood clot, vomitus, sputum plug
- In the wall, e.g. epiglottitis, laryngeal oedema, anaphylaxis, neoplasm
- Outside the wall, e.g. trauma (facial, neck), thyroid mass, haematoma

Presentation

- In spontaneously breathing patient: stridor, dyspnoea, fatigue, cyanosis
- In ventilated patient (due to intraluminal obstruction): raised airway pressures, decreased tidal volume, hypoxaemia, hypercapnia

Diagnosis

- Chest and lateral neck X-ray
- Fibreoptic laryngoscopy/bronchoscopy
- CT scan

Management

Presentation outside ICU/operating theatre:

1. High FIO_2

2. If collapsed or in extremis: immediate orotracheal intubation. If impossible, emergency cricothyroidotomy or tracheostomy.

3. If symptomatic but not *in extremis*: consider cause and treat as appropriate, e.g. fibreoptic or rigid bronchoscopy for removal of foreign body, surgery for thyroid mass. Elective orotracheal intubation or tracheostomy may be required.

4. With acute epiglottitis, the use of a tongue depressor or nasendoscopy may precipitate complete obstruction so should be undertaken in an operating theatre ready to perform emergency tracheostomy. The responsible organism is usually *Haemophilus influenzae* and early treatment with chloramphenicol should be begun. Acute epiglottitis is recognised in adults, even those of advanced age.

5. Consider Heliox (79%He/21%O_2) alone or as a supplement to oxygen to reduce viscosity and improve airflow.

Presentation within ICU/operating theatre:

1. If intubated:

   - High FIO_2

   - Pass suction catheter down the endotracheal tube, assess ease of passage and the contents suctioned. If the tube is patent, attempt repeated suction interspersed with 5ml boluses of 0.9% saline. Urgent fibreoptic bronchoscopy may be necessary for diagnosis and, if possible, removal of a foreign body. If this cannot be removed by fibreoptic bronchoscopy, urgent rigid bronchoscopy should be performed by an experienced operator. If the endotracheal tube is obstructed, remove the tube, oxygenate by face mask then reintubate.

2. If not intubated:

   - As for out-of-ICU presentation.

   - If recently extubated, consider laryngeal oedema. Post-extubation laryngeal oedema is unpredictable though occurs more commonly after prolonged or repeated intubation; the incidence may be reduced by proper tethering of the endotracheal tube and prevention of excessive coughing. If diagnosed (by nasendoscopy), dexamethasone 4mg × 3 doses over 24h may reduce the swelling though re-intubation is often necessary in the interim.

See also:

Respiratory failure
Defined as impaired pulmonary gas exchange leading to hypoxaemia and/or hypercapnia.

Commoner ICU causes

Central	Cerebrovascular accident, drugs (e.g. opiates, sedatives), raised intracranial pressure, trauma
Brainstem/spinal cord	Trauma (at or above phrenic level), tetanus, Pickwickian syndrome, motor neurone disease
Neuropathy	Guillain–Barré, critical illness polyneuropathy
Neuromuscular	Muscle relaxants, organophosphorus poisoning, myasthenia gravis
Chest wall/muscular	Flail chest, heart failure, myopathy (including critical illness and disuse myopathy)
Airways	Upper airways obstruction, airway disruption, asthma, anaphylaxis
Parenchymal	Pneumonia, ARDS, fibrosis, pulmonary oedema
Extrapulmonary	Pneumothorax, pleural effusion, haemothorax
Circulatory	Pulmonary embolus, heart failure, Eisenmenger intracardiac shunt

Types of respiratory failure

Type I: Hypoxaemic—often parenchymal in origin

Type II: Hypoxaemic, hypercapnic—often mechanical in origin

Principles of management

1. Ensure SaO_2 compatible with survival (i.e. usually >80%, preferably >90–95%)

2. Correct abnormality where possible, e.g. drain pneumothorax, relieve/bypass obstruction.

3. Support therapy until recovery

   - Positive pressure ventilation

   - Non-invasive respiratory support

   - Pharmacological treatment, e.g. bronchodilators, antibiotics, opiate antagonists, respiratory stimulant

   - General measures, e.g. hydration, airway humidification, removal of secretions, physiotherapy, bronchoscopy

4. Unless the patient is symptomatic (e.g. drowsy, dyspnoeic) while being mechanically ventilated, the $PaCO_2$ may be left elevated to minimise ventilator trauma (permissive hypercapnia).Higher $PaCO_2$ values may also be tolerated if the patient is chronically hypercapnic (Type II respiratory failure).

See also:

Atelectasis and pulmonary collapse

A collapsed lobe or segment is usually visible on a CXR. Macroatelectasis is also evident as volume loss. In microatelectasis the CXR may be normal but A-aDO$_2$ will be high. Atelectasis reduces lung compliance and PaO$_2$, and increases work of breathing. This may result in poor gas exchange, increased airway pressures, reduced tidal volume and, if severe, circulatory collapse.

Causes

- Collapsed lobe/segment—bronchial obstruction (e.g. sputum retention, foreign body, blood clot, vomitus, misplaced endotracheal tube)

- Macroatelectasis—air space compression by heavy, oedematous lung tissue, external compression (e.g. pleural effusion, haemothorax), sputum retention

- Microatelectasis—inadequate depth of respiration, nitrogen washout by 100% oxygen with subsequent absorption of oxygen occurring at a rate greater than replenishment.

Sputum retention

Excess mucous (sputum) normally stimulates coughing. If ciliary clearance is reduced (e.g. smoking, sedatives) or mucous volume is excessive (e.g. asthma, bronchiectasis, cystic fibrosis, chronic bronchitis) sputum retention may occur. Sputum retention may also be the result of inadequate coughing (e.g. chronic obstructive lung disease, pain, neuromuscular disease) or increased mucous viscosity (e.g. hypovolaemia, inadequate humidification of inspired gas).

Preventive measures

- Sputum hydration—maintenance of systemic hydration and humidification of inspired gases (e.g. nebulized saline/bronchodilators, heated water bath, heat moisture exchanging filter).

- Cough—requires inspiration to near total lung capacity, glottic closure, contraction of abdominal muscles and rapid opening of the glottis. Dynamic compression of the airways and high velocity expiration expels secretions. The process is limited if total lung capacity is reduced, abdominal muscles are weak, pain limits contraction or small airways collapse on expiration. It is usual to flex the abdomen on coughing and this should be simulated in supine patients by drawing the knees up. This also limits pain in patients with an upper abdominal wound.

- Physiotherapy—postural drainage, percussion and vibration hyperinflation, intermittent positive pressure breathing, incentive spirometry or manual hyperinflation.

- Maintenance of lung volumes—increased V_T CPAP, PEEP, positioning to reduce compression of lung tissue by oedema.

Management

Specific management depends on the cause and should be corrective. All measures taken for prevention should continue. If there is lobar or segmental collapse with obstruction of proximal airways, bronchoscopy may be useful to allow directed suction, foreign body removal and saline instillation. Patients with high FIO_2 may deteriorate due to the effects of excessive lavage or suction reducing minute ventilation.

See also:

Chronic airflow limitation

Many patients requiring ICU admission for a community acquired pneumonia have chronic respiratory failure. An acute exacerbation (which may or may not be infection-related) results in decompensation and symptomatic deterioration. Infections resulting in acute exacerbations include viruses, *Haemophilus influenzae, Klebsiella* and *Staph. aureus* in addition to *Strep. pneumoniae, Mycoplasma pneumoniae* and *Legionella pneumophila*. Otherwise, patients with coincidental chronic airflow limitation (CAL) are admitted for other reasons or as a prophylactic measure in view of their limited respiratory function, e.g. for elective post-operative ventilation.

Problems in managing CAL patients on the ICU

- Disability due to chronic ill health

- Fatigue, muscle weakness and decreased physiological reserve leading to earlier need for ventilatory support, increased difficulty in weaning, and greater physical dependency on support therapies

- Psychological dependency on support therapies

- More prone to pneumothoraces

- Usually have greater levels of sputum production

- Right ventricular dysfunction (cor pulmonale)

Notes

- Decisions on whether or not to intubate should be made in consultation with the patient (if possible), the family, and a respiratory physician with knowledge of the patient. The patient should be given the benefit of the doubt and intubated in an acute situation where a precise history and quality of life is not known.

- Trials of non-invasive ventilatory support ± respiratory stimulants such as doxepram have shown considerable success in avoiding intubation and mechanical ventilation.

- Accept lower target levels of PaO_2

- Accept higher target levels of $PaCO_2$ if patient is known or suspected to have chronic CO_2 retention on the basis of elevated plasma bicarbonate levels on admission to hospital.

Weaning the patient with CAL

- An early trial of extubation may be worthwhile before the patient becomes ventilator-dependent.

- Weaning may be a lengthy procedure. Daily trials of spontaneous breathing may reveal faster-than-anticipated progress.

- Provide plentiful encouragement and psychological support. Setting daily targets and early mobilisation may be advantageous.

- Do not tire by prolonged spontaneous breathing. Consider gradually increasing periods of spontaneous breathing interspersed by periods of rest. Ensure a good night's sleep.

- Use patient appearance and lack of symptoms (e.g. tachypnoea, fatigue) rather than specific blood gas values to judge the duration of spontaneous breathing.

- Early tracheostomy may benefit when difficulty in weaning is expected.

- The patient may cope better with a tracheostomy mask than CPAP.

- Addition of extrinsic PEEP or CPAP may prevent early airways closure and thus reduce the work of breathing. However, this should be done with caution because of the risk of increased air trapping.

- Consider heart failure as a cause of difficulty in weaning.

Key trials

Brochard L, et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. N Engl J Med 1995; 333:817–22

Antonelli M, et al. A comparison of noninvasive positive-pressure ventilation and conventional mechanical ventilation in patients with acute respiratory failure. N Engl J Med 1998; 339:429–35

Epstein SK, Ciubotaru RL. Independent effects of etiology of failure and time to reintubation on outcome for patients failing extubation. Am J Respir Crit Care Med 1998; 158:489–93

Acute chest infection (1)

Patients may present to intensive care as a result of an acute chest infection or may develop infection as a complication of intensive care management. Typical features include fever, cough, purulent sputum production, breathlessness, pleuritic pain and bronchial breathing. Urgent investigation includes arterial gases, CXR, blood count and cultures of blood and sputum. In community acquired pneumonia, acute phase antibody titres should be taken.

Diagnosis and initial antimicrobial treatment

Basic resuscitation is required if there is cardiorespiratory compromise. Appropriate treatment of the infection depends on CXR and culture findings, although empiric 'best guess' antibiotic treatment may be started before culture results are available. Treatment includes physiotherapy and methods to aid sputum clearance.

Clear CXR

Acute bronchitis is associated with cough, mucoid sputum and wheeze. In previously healthy patients a viral aetiology is most likely and there is often an upper respiratory prodrome. Symptomatic relief is usually all that is required. Likely organisms in acute on chronic bronchitis include *Strep. pneumoniae, H. in. uenzae or Staph. aureus*. Appropriate antibiotics include cefuroxime or ampicillin and .ucloxacillin. Viral pneumonia may be confused by the presence of bacteria in the sputum but secondary bacterial infection is common.

Pulmonary cavitation on CXR

Cavitation should alert to the possibility of anaerobic infection (sputum is often foul smelling). *Staph. aureus, K.*

pneumoniae or tuberculosis are also associated with cavitation. Appropriate antibiotics include metronidazole or clindamycin for anaerobic infection, flucloxacillin for *Staph. aureus* and ceftazidime and gentamicin for *K. pneumoniae*. A foreign body or pulmonary infarct should also be considered where there is a single abscess.

Consolidation on CXR

The recent history is important for deciding the cause of a pneumonia:

- Hospital acquired pneumonia—enteric (Gram negative) organisms treated with ceftazidime and gentamicin, *Staph. aureus* treated with ceftazidime and gentamicin, Staph. aureus treated with flucloxacillin (or teicoplanin/vancomycin if multiresistant).

- Recent aspiration—anaerobic or Gram negative infection treated with clindamycin or cefuroxime and metronidazole.

- Community acquired pneumonia in a previously healthy individual—*Strep. pneumoniae* (often lobar, acute onset) or atypical pneumonia (insidious onset, known community outbreaks, renal failure and electrolyte disturbance in Legionnaire's disease). Appropriate antibiotic therapy is cefuroxime and clarithromycin.

- Pneumonia complicating influenza—*Staph. aureus* treated with flucloxacillin. Both *Staph. aureus* and *H. influenzae* are common in those debilitated by chronic disease (e.g. alcoholism, diabetes, chronic airflow limitation or the elderly).

- Immunosuppressed—opportunistic infections (e.g. tuberculosis, *Pneumocystis carinii* Herpes viruses, CMV or fungi).

Antimicrobial treatment

Drug	Dose	Organism
Acyclovir	10mg/kg 8-hrly IV	*Herpes viruses*
Amphotericin B	250mg–1g 6-hrly IV	Fungi
Ampicillin	500mg–1g 6-hrly IV	*H. influenzae* Gram negative spp.
Benzylpenicillin	1.2g 2–6-hrly IV	*Strep. pneumoniae*
Ceftazidime	2g 8-hrly IV	*K. pneumoniae* *Ps. aeruginosa* Gram negative spp.
Cefuroxime	750mg–1.5g 8-hrly IV	*Strep. pneumoniae* *H. influenzae* Gram negative spp.
Clarithromycin	500mg 12-hrly IV (250–500mg 12-hrly PO if less severe)	Atypical pneumonia *Strep. pneumoniae*
Erythromycin	1g 6–12-hrly (500mg 6-hrly PO if less severe)	Atypical pneumonia *Strep. pneumoniae*
Clindamycin	300–600mg 6-hrly IV	Anaerobes Gram negative spp.
Cotrimoxazole	120mg/kg/day IV	*Pneumocystis carinii*
Flucloxacillin	2g 6-hrly IV (500mg–1g 6-hrly PO if less severe)	*Staph. aureus*
Ganciclovir	5mg/kg 12-hrly IV (over 1h)	CMV
Gentamicin	1.5mg/kg stat IV(thereafter by levels—usually 80mg 8-hrly)	*K. pneumoniae, Ps. aeruginosa* Gram negative spp.
Metronidazole	500mg 8-hrly IV or 1g 12-hrly PR	Anaerobes
Teicoplanin	400mg 12-hrly for 3 doses then 400mg daily	Methicillin-resistant *Staph. aureus*
Vancomycin	500mg 6-hrly (monitor levels)	Methicillin-resistant *Staph. aureus*
Linezolid	600mg 12-hrly IV or PO	Methicillin-resistant *Staph. aureus*

Key trial

Iregui M et al. Clinical importance of delays in the initiation of appropriate antibiotic treatment for ventilator-associated pneumonia. Chest 2002; 122: 262–8

Acute chest infection (2)

Laboratory diagnosis

The following samples are required for laboratory diagnosis:

- Sputum (e.g. cough specimen, endotracheal tube aspirate, protected brush specimen, bronchoalveolar lavage specimen)
- Blood cultures
- Serology (in community acquired pneumonia)

- Urine for antigen tests (if *Legionella, Candida* or pneumococcus suspected)

In severe pneumonia, blind antibiotic therapy should not be withheld while awaiting results. Specimens should, however, be taken before starting antibiotics.

Microbiological yield is usually very low, especially if antibiotic therapy has started before sampling.

Where cultures are positive there is often multiple growth. Separating pathogenic organisms from colonising organisms may be difficult.

In hospital acquired pneumonia, known nosocomial pathogens are the likely source, e.g local Gram negative flora, MRSA.

Continuing treatment

Antibiotics should be adjusted according to sensitivities once available. Failure to respond to treatment in 72h should prompt consideration of infections more common in the immunocompromised or other diagnoses.

Hospital-acquired pneumonia requires treatment with appropriate antibiotics for 24h after symptoms subside (usually 3–5 days). After this period cultures should be repeated (off antibiotics if there has been improvement). Some ICUs will use longer courses—a recent multicentre study showed no difference in outcome between 8 and 15 days' treatment.

In atypical or pneumococcal pneumonia, 10–14 days of antibiotic treatment is usual (though no evidence base exists to indicate the optimal duration of therapy).

Key trial

Chastre J, for the PneumA Trial Group. Comparison of 8 vs 15 days of antibiotic therapy for ventilator-associated pneumonia in adults: a randomized trial. JAMA 2003; 290:2588–98

Acute respiratory distress syndrome (1)

ARDS is the respiratory component of multiple organ dysfunction. It may be predominant in the clinical picture or be of lesser clinical importance in relation to dysfunction of other organ systems.

Aetiology

As part of the exaggerated inflammatory response following a major exogenous insult which may be either direct (e.g. chest trauma, inhalation injury) or distant (e.g. peritonitis, major haemorrhage, burns). Histology reveals aggregation and activation of neutrophils and platelets, patchy endothelial and alveolar disruption, interstitial oedema and fibrosis. Classically, the acute phase is characterised by increased capillary permeability and the fibroproliferative phase (after 7 days) by a predominant fibrotic reaction. However, more recent data would suggest such distinctions are not so clear-cut; there may be evidence of markers of fibrosis as early as day 1.

Definitions

Acute lung injury (ALI)

- $PaO_2/FIO_2 \leq 300mmHg$ (40kPa)
- Regardless of level of PEEP
- With bilateral infiltrates on CXR
- With pulmonary artery wedge pressure <18mmHg

Acute respiratory distress syndrome (ARDS)

As above but $PaO_2/FIO_2 \leq 200mmHg$ (26.7kPa)

Prognosis

Prognosis depends in part on the underlying insult, the presence of other organ dysfunctions and the age and chronic health of the patient. Predominant single-organ ARDS carries a mortality of 30–50%; there does appear to have been some improvement over the last decade.

Some deterioration on lung function testing is usually detectable in survivors of ARDS, even in those who are relatively asymptomatic. Recent studies indicate that a significant proportion of survivors of ARDS have physical and/or psychological sequelae at 1 year.

Key trials

Bernard GR for the The American–European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. Am J Respir Crit Care Med. 1994; 149:818–24

Herridge MS, Cheung AM for the Canadian Critical Care Trials Group. One-year outcomes in survivors of the acute respiratory distress syndrome. N Engl J Med 2003; 348:683–93

Marshall RP, et al. Fibroproliferation occurs early in the acute respiratory distress syndrome and impacts on outcome. Am J Respir Crit Care Med 2000; 162:1783–8

See also:

Acute respiratory distress syndrome (2)

General management

1. Remove the cause whenever possible, e.g. drain pus, antibiotic therapy, fix long bone fracture.

2. Sedate with an opiate–benzodiazepine combination as mechanical ventilation is likely to be prolonged. Doses should be kept to the lowest possible but consistent with adequate sedation.

3. Muscle relaxation is indicated in severe ARDS to improve chest wall compliance and gas exchange.

4. Haemodynamic manipulation with either fluid, dilators, pressors, diuretics and/or inotropes may improve oxygenation. This may be achieved by either increasing cardiac output, and thus mixed venous saturation in low output states, or by decreasing cardiac output thereby lengthening pulmonary transit times in high output states. Care should be taken not to compromise the circulation.

Respiratory management

1. Maintain adequate gas exchange with increased FIO_2 and, depending on severity, either non-invasive respiratory support (e.g. CPAP, BiPAP) or positive pressure ventilation. Specific modes may be utilised, such as pressure controlled inverse ratio ventilation. While general agreement exists for minimising VT (6-7ml/kg) and plateau inspiratory pressures ($\leq$30cmH$_2$O) if possible, there is no consensus regarding the upper desired level of FIO_2 and PEEP. Greater emphasis is currently placed on higher levels of PEEP (up to 20cm H$_2$O) While the current European view favours the use of higher FIO_2 (up to 1.0), a common US approach is to keep the FIO_2 $\leq$0.60 but to maintain SaO$_2$ with higher levels of PEEP. A recent study assessing higher levels of PEEP showed no outcome benefit.

2. Non-ventilatory respiratory support techniques such as ECCO$_2$R can be used in severe ARDS but have yet to show convincing benefit over conventional ventilatory techniques.

3. Blood gas values should be aimed at maintaining survival without striving to achieve normality. Permissive hypercapnia, where PaCO$_2$ values are allowed to rise, sometimes above 10kPa, has been associated with outcome benefit. Acceptable levels of SaO$_2$ are controversial; in general, values $\geq$90–95% are targeted but in severe ARDS this may be relaxed to 80–85% or even lower provided organ function remains adequate.

4. Patient positioning may provide improvements in gas exchange. This includes kinetic therapy using special rotational beds, and prone positioning with the patient being turned frequently through 180°. Care has to be taken during prone positioning to prevent tube displacement and shoulder injuries.

5. Inhaled nitric oxide or epoprostenol improves gas exchange in some 50% of patients, though no outcome benefit has been shown.

6. High dose steroids commenced at 7–10 days are beneficial in 50–60% of patients, at least in terms of improving gas exchange.

7. Surfactant therapy is currently not indicated for ARDS.

8. Ventilator trauma is ubiquitous. Multiple pneumothoraces are common and may require multiple chest drains. They may be difficult to diagnose by X-ray and, despite the attendant risks, CT scanning may reveal undiagnosed pneumothoraces and aid correct siting of chest drains.

Key trials

Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000; 342:1301–8

Hickling KG, et al. Low mortality rate in adult respiratory distress syndrome using low-volume, pressure-limited ventilation with permissive hypercapnia: a prospective study. Crit Care Med 1994; 22:1568–78

Meduri GU, et al. Effect of prolonged methylprednisolone therapy in unresolving acute respiratory distress syndrome: a randomized controlled trial. JAMA 1998; 280:159–65

Gattinoni L, et al for the Prone-Supine Study Group. Effect of prone positioning on the survival of patients with acute respiratory failure. N Engl J Med 2001; 345:568–73

See also:

Oxygen therapy, p2; Ventilatory support—indications, p4; IPPV—complications of ventilation, p14; Positive end expiratory pressure (1) Positive end expiratory pressure (2), p24; Continuous positive airway pressure, p26; Lung recruitment, p28; Prone positioning, p30; Extracorporeal respiratory support, p34; Endotracheal intubation, p36; Blood gas analysis, p100; Bacteriology, p158; Virology, serology and assays, p160; Colloid osmotic pressure, p172; Colloids, p180; Bronchodilators, p186; Nitric oxide, p190; Surfactant, p192; Antimicrobials, p260; Steroids, p262; Basic resuscitation, p270; Acute chest infection (1), p288; Acute chest infection (2), p290; Acute respiratory distress syndrome (2), p294; Inhalation injury, p306; Infection—diagnosis, p480; Infection—treatment, p482; Systemic inflammation/multiorgan failure, p484; Sepsis and septic shock—treatment, p486; Multiple trauma (1), p500; Multiple trauma (2), p502; Pyrexia (1), p518; Pyrexia (2), p520

Asthma—general management

Pathophysiology

Acute bronchospasm and mucus plugging, often secondary to an insult such as infection. The patient may progress to fatigue, respiratory failure and collapse. The onset may develop slowly over days, or occur rapidly within minutes to hours.

Clinical features

- Dyspnoea, wheeze (expiratory ± inspiratory), difficulty in talking, use of accessory respiratory muscles, fatigue, agitation, cyanosis, coma, collapse.

- Pulsus paradoxus is a poor indication of severity; a fatiguing patient cannot generate significant respiratory swings in intrathoracic pressure.

- A 'silent' chest is also a late sign suggesting severely limited airflow.

- Pneumothorax and lung/lobar collapse.

Management of asthma

Asthmatics must be managed in a well-monitored area. If clinical features are severe, they should be admitted to an intensive care unit where rapid institution of mechanical ventilation is available. Monitoring should comprise, as a minimum, pulse oximetry, continuous ECG, regular blood pressure measurement and blood gas analysis. If severe, an intra-arterial cannula ± central venous access should be inserted.

1. High FIO_2 (≥ 0.60) to maintain $SpO_2 \geq 95\%$.

2. Nebulised β_2-agonist (e.g. salbutamol)—may be repeated every 2–4h or, in severe attacks, administered continuously

3. IV steroids for 24h then oral prednisolone. Nebulised ipratropium bromide may give additional benefit.

4. IV bronchodilators, e.g. salbutamol, magnesium sulphate.

5. Exclude pneumothorax and lung/lobar collapse.

6. Ensure adequate hydration and fluid replacement.

7. Commence antibiotics (e.g. cefuroxime ± clarithromycin) if strong evidence of bacterial chest infection. Green sputum does not necessarily indicate a bacterial infection.

8. If no response to above measures or *in extremis* consider:
   - IV salbutamol infusion
   - Epinephrine SC or by nebuliser
   - Mechanical ventilation
   - Anecdotal success has been reported with subanaesthetic doses of a volatile anaesthetic agent such as isoflurane which both calms/sedates and bronchodilates.

Indications for mechanical ventilation

- Increasing fatigue and obtundation
- Respiratory failure—rising $PaCO_2$ falling PaO_2
- Cardiovascular collapse

Facilitating endotracheal intubation

Summon senior assistance. Pre-oxygenate with 100% O_2. Perform rapid sequence induction with suxamethonium and etomidate or ketamine. 'Breathing down' with an inhalational anaesthetic (e.g. isoflurane) pre- intubation should only be attempted by an experienced clinician. To minimse barotrauma, care should be taken to avoid excess air trapping, high airway pressures and high tidal volumes.

Drug dosage

Epinephrine	0.5ml 1:1000 solution SC or 2ml 1:10,000 solution by nebuliser
Hydrocortisone	100–200mg qds
Ipratropium bromide	250–500µg qds by nebuliser
Prednisolone	40–60mg od initially
Salbutamol	2.5–5mg by nebuliser 5–20µg/min by IV infusion
Magnesium sulphate	1.2–2.0g IV over 20min

See also:

Oxygen therapy, p2; Ventilatory support—indications, p4; Endotracheal intubation, p36; Pulse oximetry, p90; Blood gas analysis, p100; Bacteriology, p158; Bronchodilators, p186; Sedatives, p238; Steroids, p262; Dyspnoea, p278; Asthma—ventilatory management, p298; Anaphylactoid reactions, p496

Asthma—ventilatory management

Early period

1. Initially give low V_T (5ml/kg) breaths at low rate (5–10/min) to assess degree of bronchospasm and air trapping. Slowly increase V_T (to 7-8ml/kg) ± increase rate, taking care to avoid significant air trapping and high inspiratory pressures. Low rates with prolonged I:E ratio (e.g. 1:1) may be advantageous. Avoid very short expiratory times.Do not strive to achieve normocapnia.

2. Administer muscle relaxants for a minimum 2–4h, until severe bronchospasm has abated and gas exchange improved. Although atracurium may cause histamine release, it does not appear clinically to worsen bronchospasm.

3. Sedate with either standard medication or with agents such as ketamine or isoflurane that have bronchodilating properties. Ketamine given alone may cause hallucinations while isoflurane carries a theoretical risk of fluoride toxicity.

4. If significant air trapping remains, consider ventilator disconnection and forced manual chest compressions every 10–15min

5. If severe bronchospasm persists, consider injecting 1–2ml of 1:10,000 epinephrine down endotracheal tube. Repeat at 5min intervals as necessary.

Maintenance

1. Ensure adequate rehydration.

2. Generous humidification should be given to loosen mucus plugs. Use a heat–moisture exchanger plus either hourly 0.9% saline nebulisers or instillation of 5ml 0.9% saline down the endotracheal tube.

3. Physiotherapy assists mobilisation of secretions and removal of mucus plugs. Hyperventilation should be avoided.

4. With improvement, gradually normalise ventilator settings (V_T, rate, I:E ratio) to achieve normocapnia before allowing patient to waken and breathe spontaneously

5. Consider pneumothorax or lung/lobar collapse if acute deterioration occurs.

6. If mucus plugging constitutes a major problem, instillation of a mucolytic (*N*-acetyl cysteine) may be considered though this may induce further bronchospasm. Bronchoscopic removal of plugs should only be performed by an experienced operator.

Assessment of air trapping (intrinsic PEEP, PEEPi)

- Measure PEEPi by pressing end-expiratory hold button of ventilator.
- No pause between expiratory and inspiratory sounds.
- Disconnection of ventilator and timing of audible expiratory wheeze.
- An increasing $PaCO_2$ may respond to reductions in minute volume which will lower the level of intrinsic PEEP.

Weaning

- Bronchospasm may increase on lightening sedation due to awareness of endotracheal tube and increased coughing.
- May need trial of extubation while still on high FIO_2
- Consider extubation under inhalational or short-acting IV sedation.

space out intervals between β_2 agonist nebulisers. Convert other antiasthmatic drugs to oral medication. Theophylline doses should be adjusted to ensure therapeutic levels.

See also:

Pneumothorax

Significant collection of air in the pleural space that may occur spontaneously, following trauma (including iatrogenic), asthma, chronic lung disease, and is a common sequel of ventilator trauma.

Clinical features

- May be asymptomatic.
- Dyspnoea, pain.
- Decreased breath sounds, hyper-resonant, asymmetric chest expansion—may be difficult to assess in a ventilated patient.
- Respiratory failure and deterioration in gas exchange.
- Increasing airway pressures and difficulty to ventilate.
- Cardiovascular deterioration with mediastinal shift (tension).

Diagnosis

- CXR—most easily seen on erect views where absent lung markings are seen lateral to a well-defined lung border. However, ventilated patients are often imaged in a supine position; pneumothorax may be easily missed as it may be lying anterior to normal lung giving the misleading appearance of lung markings on the radiograph. Supine pneumothorax should be considered if the following are seen:
  - Hyperlucent lung field compared to the contralateral side
  - Loss of clarity of the diaphragm outline
  - 'Deep sulcus' sign, giving the appearance of an inverted diaphragm
  - A particular clear part of the cardiac contour
  - A lateral film may help. Tension pneumothorax results in marked mediastinal shift away from the affected side.
  - Ultrasound—may be helpful but is highly operator dependent
  - CT scan—very sensitive and may be useful in difficult situations, e.g. ARDS, and to direct drainage of localised pneumothorax

Pneumothorax must be distinguished from bullae, especially with long-standing emphysema; inadvertent drainage of a bulla may cause a bronchopleural fistula. Assistance should be sought from a radiologist.

Management

1. Increase FIO_2 if hypoxaemic.
2. If life-threatening with circulatory collapse, needle aspirate pleura on affected side, followed by formal chest

drain insertion.

3. Repeated needle aspiration may be sufficient in spontaneously breathing patients without respiratory failure; however, this is not recommended if the patient is ventilated.

4. Chest drain insertion. This may be done under ultrasound or CT guidance, especially if localised due to surrounding lung fibrosis.

A small pneumothorax (<10% hemithorax) may be left undrained but prompt action should be instituted if cardiorespiratory deterioration occurs. Patients should not be transferred between hospitals, particularly by plane, with an undrained pneumothorax. Drains may be removed if not swinging/bubbling for several days.

Bronchopleural fistula

Denoted by continual drainage of air. Usually responds to conservative treatment with continual application of 5kPa negative pressure; this may take weeks to resolve. For severe leak and/or compromised ventilation, high frequency jet ventilation and/or a double lumen endobronchial tube may be considered. Surgical intervention is rarely necessary.

Chest X-ray appearance

rim of air on erect X-ray
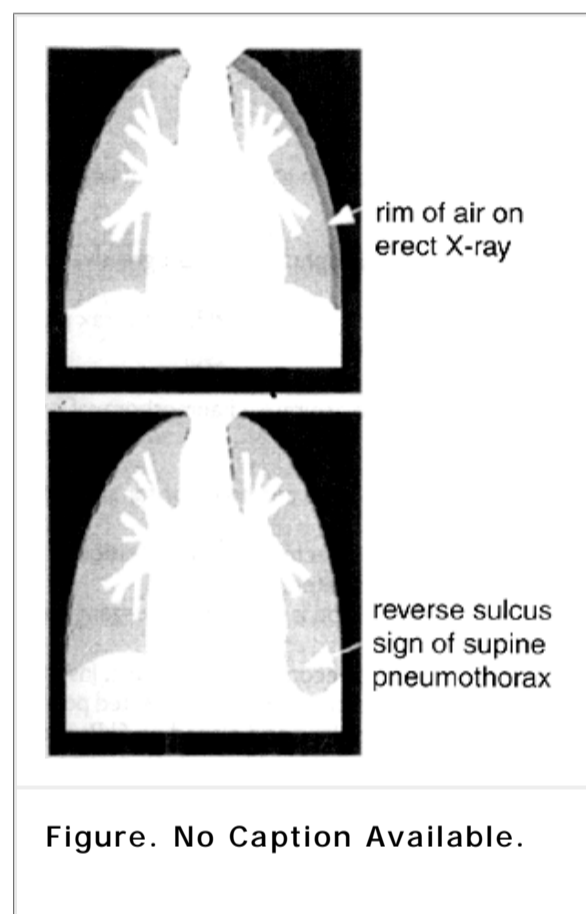
reverse sulcus sign of supine pneumothorax

Figure. No Caption Available.

See also:

IPPV—complications of ventilation, p14; High frequency ventilation, p20; Chest drain insertion, p42; Central venous catheter—insertion, p116; Basic resuscitation, p270; Respiratory failure, p282; Acute respiratory distress syndrome (1), p292; Acute respiratory distress syndrome (2), p294; Multiple trauma (1), p500; Multiple trauma (2), p502

Haemothorax

Usually secondary to chest trauma or following a procedure, e.g. cardiac surgery, chest drain insertion, central venous catheter insertion. Spontaneous haemothorax is very rare, even in patients with clotting disorders.

Clinical features

- Stony dullness.
- Decreased breath sounds.
- Hypovolaemia and deterioration in gas exchange (if large).

Diagnosis

- Erect CXR—blunting of hemidiaphragm and progressive loss of basal lung field
- Supine CXR—increased opacity of affected hemithorax plus decreased clarity of cardiac contour on that side.
- Large bore needle aspiration to confirm presence of blood. A small bore needle may be unable to aspirate a haemothorax if it has clotted.

Management

1. If small, observe with serial X-rays and monitor for signs of cardiorespiratory deterioration.

2. Ensure any coagulopathy is corrected by administration of fresh frozen plasma and/or platelets as indicated.

3. Ensure that cross-matched blood is available for urgent transfusion if necessary.

4. If significant in size or patient becomes symptomatic, insert large bore chest drain, e.g. size 28 Fr. The drain should be directed postero-inferiorly toward the dependent area of lung and placed on 5kPa suction.

5. If drainage exceeds 1000ml or >200ml/h for 3–4h despite correcting any coagulopathy, contact thoracic surgeon.

6. Factor VIIa may be considered for intractable bleeding, though only anecdotal reports of benefit exist.

7. Drains inserted for a haemothorax may be removed after 1–2 days if no further bleeding occurs.

Perforation of an intercostal vessel during chest drain insertion may cause considerable bleeding into the pleura. If deep tension sutures around the chest drain fail to stem blood loss, remove the chest drain and insert a Foley urethral catheter through the hole. Inflate the balloon and apply traction on the catheter to tamponade the bleeding vessel. If these measures fail, contact a thoracic surgeon.

See also:

Haemoptysis

- May range from a few specks of blood in expectorated sputum to massive pulmonary haemorrhage.

- More likely to disrupt gas exchange before life-threatening hypovolaemia ensues.

- May be a presenting feature of a patient admitted to intensive care or may result from critical illness and its treatment.

Causes

Massive haemoptysis

- Disruption of a bronchial artery by acute inflammation or invasion (e.g. pulmonary neoplasm, trauma, cavitating TB, bronchiectasis, lung abscess and aspergilloma).

- Rupture of arteriovenous malformations and bronchovascular fistulae.

- Pulmonary infarction secondary to prolonged pulmonary artery catheter wedging or pulmonary artery rupture.

Minor haemoptysis

- Intrapulmonary inflammation or infarction (e.g. pulmonary embolus)

- Endotracheal tube trauma (e.g. mucosal erosion, balloon necrosis, trauma from the tube tip, trauma to a tracheostomy stoma, trauma from suction catheters).

- Tissue breakdown in critically ill patients (e.g. tissue hypoperfusion, coagulopathy, poor nutritional state, sepsis and hypoxaemia.)

Investigation and assessment

Urgent assessment of cardiorespiratory function and cardiorespiratory monitoring are required. Massive haemoptysis may require resuscitation and urgent intubation. The diagnosis may be suggested by the history and a CXR may identify a cavitating lesion. Lower lobe shadowing on a CXR may be the result of overspill of blood from elsewhere in the bronchial tree. Early surgical intervention should be prompted by a changing air-fluid level, persistent opacification of a previous cavity or a mobile mass. Early bronchoscopy may identify the source of haemoptysis, although only while bleeding is active. Blood in multiple bronchial orifices may be confusing but saline lavage may leave the source visible. Rigid bronchoscopy is useful in massive haemoptysis allowing oxygenation and wide bore suction.

Management

- Basic resuscitation (high FIO_2, endotracheal intubation and bloodtransfusion) is needed for cardiorespiratory compromise.

- Correction of coagulopathy is a priority.

- Bronchoscopy allows direct instillation of 1 in 200,000 epinephrine if the source of haemorrhage can be found or,

alternatively, endobronchial tamponade with a balloon catheter.

- In cases of severe haemorrhage from one lung a double lumen endotracheal tube may prevent some overspill to the other lung while definitive treatment is organised.

- Definitive treatment may include radiological bronchial artery embolisation, or surgical resection.

- Induced hypotension may be useful in bronchial artery haemorrhage.

- In cases of pulmonary artery haemorrhage, PEEP may be used with mechanical ventilation to reduce pulmonary bleeding.

See also:

Inhalation injury
Causes include smoke, steam, noxious gases and aspiration of gastric contents.

Clinical features

- Dyspnoea, coughing

- Stridor (if upper airway obstruction)

- Bronchospasm

- Signs of lung/lobar collapse (especially with aspiration)

- Signs of respiratory failure

- Cherry-red skin colour (carbon monoxide)

- Agitation, coma

- ARDS (late)

General principles of management

1. 100% O_2

2. Early intubation if upper airway compromised or threatened.

3. Early bronchoscopy if inhalation of soot, debris, vomit suspected.

Specific conditions

Smoke inhalation

- Smoke rarely causes thermal injury beyond the level of bronchi as it has a low specific heat content. However, soot is a major irritant to the upper airways and can produce very rapid and marked inflammation.

- Urgent laryngoscopy should be performed if soot is present in the nares, mouth or pharynx.

- If soot is seen or the larynx appears inflamed, perform early endotracheal intubation. As the upper airway can obstruct within minutes it is advisable to intubate as a prophylactic measure rather than as an emergency where it may prove impossible.

- After intubation, perform urgent bronchoscopy with bronchial toilet using warmed 0.9% saline to remove as much soot as possible.

- Commence benzylpenicillin 1.2g qds IV.

- Specific treatment for poisons contained within smoke (e.g. carbon monoxide, cyanide)

Steam inhalation

- Consider early/prophylactic intubation

- Steam has a much higher heat content than smoke and can cause injury to the whole respiratory tract.

- Consider early bronchoscopy and lavage with cool 0.9% saline.

Aspiration of gastric contents

- Early bronchoscopy and physiotherapy to remove as much particulate and liquid matter as possible.

- Either cefuroxime plus metronidazole, or clindamycin for 3–5 days.

- Steroid therapy has no proven benefit.

See also:

Oxygen therapy, p2; Ventilatory support—indications, p4; Endotracheal intubation, p36; Fibreoptic bronchoscopy, p46; Blood gas analysis, p100; Antimicrobials, p260; Airway obstruction, p280; Inhaled poisons, p466; Burns—fluid management, p510; Burns—general management, p512

Pulmonary embolus

Aetiology

- Usually arises from a deep vein thrombosis in femoral or pelvic veins. The risk increases after prolonged immobilisation and with polycythaemia or hyperviscosity disorders.

- Amniotic fluid embolus.

- Fat embolus after pelvic or long bone trauma.

- Right heart source, e.g. mural thrombus.

Clinical features

- Pleuritic-type chest pain, dyspnoea, ± haemoptysis.

- The patient with a major embolus often prefers to lie flat. Dyspnoea improves due to increased venous return and right heart loading.

- Deterioration in gas exchange—may find a low PaO_2 low or high $PaCO_2$ and a metabolic acidosis. However, these .ndings are inconsistent and non-diagnostic.

- Cardiovascular features, e.g. tachycardia, low/high BP and collapse.

- CXR: may be normal but a massive embolus may produce fewer vascular markings (pulmonary oligaemia) in a hemithorax ± a bulging pulmonary hilum. A wedge-shaped peripheral pulmonary infarct may be seen after a few days following a smaller embolus.

- ECG: acute right ventricular strain, i.e. $S_1 Q_3 T_3$, tachycardia, right axis deviation, right bundle branch block, P pulmonale.

- Echocardiogram: may reveal evidence of pulmonary hypertension and acute right ventricular strain.

- D-dimers—though a raised level is non-diagnostic, a normal value carries a high probability of exclusion of a pulmonary embolus.

Definitive diagnosis

- CT scan with contrast—the investigation of choice for major embolus.

- Pulmonary angiography

- Ventilation–perfusion scan—degree of certainty is reduced if area of non-perfused lung corresponds to any CXR abnormality.

- Fat globules or foetal cells in pulmonary artery blood may be found in fat and amniotic fluid embolus, respectively.

General management

1. FIO_2 0.6–1.0 to maintain SaO2 ≥90–95%

2. Lie patient flat; improvement often follows increased venous return.

3. Fluid challenge to optimise right heart filling.

4. Epinephrine infusion if circulation still compromised.

5. Mechanical ventilation may be needed if the patient tires or cannot maintain adequate oxygenation. Gas exchange may worsen due to loss of preferential shunting and decreases in cardiac output.

Management of blood clot embolus

Start anticoagulation with low molecular weight heparin adjusted for weight. Consider thrombolysis if there is a major embolus and cardiovascular compromise, and embolectomy if the patient remains moribund. Otherwise, at 24–48h

commence warfarin but continue heparin for further 2–3 days after adequate oral dosing.

Management of fat embolus

Other than general measures including oxygenation, fluid resuscitation and right heart loading, treatment remains controversial. Various authorities advocate steroids, heparinisation or no specific therapy.

Low molecular weight heparin regimen

Subcutaneous low molecular weight heparin is given until oral anticoagulant therapy is fully established.

Dalteparin

200 units/kg (max. 18,000units) every 24h (or 100units/kg twice daily if increased risk of haemorrhage)

Enoxaparin

1.5mg/kg (150units/kg) every 24h

Tinzaparin

175units/kg once daily

Thrombolytic regimens

rt-PA (100mg over 90min) should be given followed by a heparin infusion (24,000–36,000units/day) to maintain the partial thromboplastin time at 2–3 × normal. This is the treatment of choice if surgery or angiography is contemplated.

Streptokinase (500,000units as a loading dose over 30min followed by 100,000units/h for 24h).

NB: Central venous catheters should ideally be inserted prethrombolysis by an experienced operator to minimise the risk of bleeding/haematoma.

Key trials

Konstantinides S, for the Management Strategies and Prognosis of Pulmonary Embolism-3 Trial Investigators. Heparin plus alteplase compared with heparin alone in patients with submassive pulmonary embolism. N Engl J Med 2002; 347:1143–50

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Cardiovascular Disorders

Hypotension

The overall principle in the management of hypotension is to maintain the minimum mean arterial pressure that will ensure adequate tissue perfusion. A normal blood pressure does not guarantee an adequate cardiac output and circulatory support should aim to achieve adequate blood flow as well. In *extremis*, the .rst line treatment options should include external cardiac massage and epinephrine 0.05–0.2mg intravenous boluses (1mg in cardiac arrest).

Assessment of hypotension

Hypotension requires treatment if the mean BP <60mmHg (higher if the patient was previously hypertensive) with signs of poor tissue perfusion (e.g. oliguria, confusion, altered consciousness, cool peripheries, metabolic acidosis). Specific treatment should be considered for haemorrhage, acute myocardial infarction, arrhythmias, pulmonary embolus, cardiac tamponade, pneumothorax, anaphylaxis, diarrhoea and vomiting, ketoacidosis, hypoadrenalism, hypopituitarism and poisoning.

Initial treatment of hypotension

Most cases of hypotension require fluid as first-line management to confirm an adequate circulating volume. Exceptions may include acute heart failure, arrhythmias, cardiac tamponade and pneumothorax. In cases of life-threatening haemorrhage group specific or O negative blood should be used urgently.

Pharmacological treatment

If hypotension persists after an adequate circulating volume, rate and rhythm has been restored, the appropriate choice of drug treatment depends on whether there is myocardial failure (signs of low output or measured low stroke

volume) or peripheral vascular failure (warm, vasodilated periphery or measured normal stroke volume). A low stroke volume should be treated with an inotrope (e.g. epinephrine, dobutamine) and peripheral vascular failure with a vasopressor (e.g. norepinephrine).

Inotropic support

Epinephrine (started at 0.2µg/kg/min), dopamine or dobutamine (started at 5µg/kg/min) should be titrated against stroke volume (if monitored). Most hypotensive patients requiring inotropes should have a pulmonary artery catheter inserted. The alternative is to titrate against blood pressure, but there is a danger of producing inappropriate vasoconstriction. Dobutamine is safer in this respect but has the disadvantage of producing excessive vasodilatation in some patients.

Vasopressors

Once stroke volume has been optimised, norepinephrine (started at 0.05µg/kg/min) should be titrated against mean BP. In most patients, with previously normal blood pressure, 60mmHg is an adequate target but may need to be higher to ensure organ perfusion in the elderly and those with previous hypertension. Norepinephrine may reduce cardiac output. This effect should be monitored and corrected by adjustment of dose. Vasopressin (or its synthetic analogue, terlipressin) is increasingly used for high output, catecholamine-resistant, vasodilatory shock. Care should be taken to avoid excessive peripheral constriction or impairment of organ perfusion.

See also:

Hypertension

Often defined in adult patients as a diastolic pressure >95mmHg and a systolic pressure >180mmHg.

Common causes in intensive care

- Idiopathic/essential

- Agitation/pain, especially where muscle relaxants are used

- Excessive vasoconstriction, e.g. cold, vasopressor drugs

- Head injury, cerebrovascular accidents

- Drug-related

- Dissecting aneurysm, aortic coarctation

- Vasculitis, thrombotic thrombocytopenic purpura

- (Pre-)eclampsia

- Aortic coarctation (may present acutely in adulthood)

- Endocrine, e.g. phaeochromocytoma (rare)

- Renal failure, renal artery stenosis (rare)

- Spurious—underdamped transducer system

Indications for acute treatment

Hypertensive encephalopathy, heart failure, eclampsia and acute dissecting aneurysm are the prime indications for rapid and aggressive, albeit controlled, reduction of blood pressure.

In other conditions, especially chronic hypertension and following acute neurological events, e.g. head injury, cerebrovascular accidents, a precipitate reduction in blood pressure may adversely affect perfusion leading to further deterioration. Hypertension post-cerebral event is not usually treated unless very high, e.g. mean BP >140–150mmHg, systolic BP >220–230mmHg. In this instance, controlled and partial reduction is mandatory, e.g. using sodium nitroprusside infusion with continuous invasive monitoring. In the presence of a raised ICP, a cerebral perfusion pressure ≥60–70mmHg is usually targeted.

Hypertensive crisis

This occurs when the patient becomes symptomatic (increasing drowsiness, seizures, papilloedema, retinopathy) in the presence of elevated systemic pressures. The diastolic BP usually exceeds 120–130mmHg and the mean BP >140–150mmHg, although encephalopathy can occur at lower pressures.

Principles of management

1. Adequate monitoring (invasive BP, ECG, CVP, CO, urine output)

2. Consider pain, hypovolaemia, hypothermia and agitation, especially if paralysed.

3. Consider specific treatment for, e.g. phaeochromocytoma, thyroid crisis, aortic dissection, inflammatory vasculitis

4. Slow intravenous infusion of nitrate or nitroprusside. GTN is usually given first before considering sodium nitroprusside. Other options include labetalol or esmolol infusions, and hydralazine (IV or IM). Sublingual nifedipine or IV hydralazine may sometimes produce precipitate falls in BP. Use cautiously and start with low doses.

5. Aim to reduce to mildly hypertensive levels unless a dissecting aneurysm is present where systolic BP should be lowered <100–110mmHg. After certain types of surgery (e.g. cardiac, aortic), control of systolic blood pressure <100–120mmHg may be requested to reduce risk of bleeding.

6. Longer term treatment, e.g. an oral ACE inhibitor, should be instituted with caution, starting at low doses.

Drug doses

Drug	Dose
GTN	0.5–20mg/h
Sodium nitroprusside	0.5–1.5µg/kg/min, increased slowly to 0.5–8.0g/kg/min
Labetolol	50mg IV over 1min repeated every 5min to maximum 200mg
Esmolol	50–200µg/min
Hydralazine	5–10mg slow IV followed by 50–150µg/min

See also:

IPPV—failure to tolerate ventilation, p12; Blood pressure monitoring, p110; Intracranial pressure monitoring, p134; Vasodilators, p198; Hypotensive agents, p202; Opioid analgesics, p234; Non-opioid analgesics, p236; Sedatives, p238; Intracranial haemorrhage, p376; Subarachnoid haemorrhage, p378; Raised intracranial pressure, p382; Pain, p532; Pre-eclampsia and eclampsia, p538; HELLP syndrome, p540

Tachyarrhythmias

If pulses are not palpable or there is severe hypotension, a tachyarrhythmia requires cardiac massage and urgent DC cardioversion. Otherwise, the initial treatment prior to diagnosis includes correction of hypoxaemia, potassium (to ensure a plasma K^+ >4.5mmol/l) and magnesium (often to levels of 1.5–2mmol/l).

Causes of tachyarrhythmias

Where possible the cause of a tachyarrhythmia should be treated. Common causes for which specific treatment may be required include hypovolaemia, hypotension (may also be due to the arrhythmia), acute myocardial infarction, pain, anaemia, hypercapnia, fever, anxiety, thyrotoxicosis and digoxin toxicity.

Diagnosis of tachyarrhythmias

Broad complex tachycardia

Regular complexes with AV dissociation (fusion beats, capture beats, QRS>140ms, axis<-30°, concordance) suggest ventricular tachycardia. If there is no AV dissociation the arrhythmia is probably supraventricular with aberrant conduction; adenosine may be used as a diagnostic test since SVT may respond and VT will not. Irregular broad complexes are probably atrial fibrillation with aberration. Torsades de pointes is a form of ventricular tachycardia with a variable axis.

Narrow complex tachycardia

The absence of P waves suggests atrial fibrillation. A P wave rate >150 is suggestive of SVT whereas slower P wave rates may represent a sinus tachycardia or atrial flutter with block. The P waves are abnormal (flutter waves) in atrial flutter and QRS complexes may be irregular if the block is variable. Extremely fast SVT may be due to a re-entry pathway with retrograde conduction and premature ectopic atrial excitation. In Wolff–Parkinson–White syndrome the re-entry pathway inserts below the His bundle allowing rapid AV conduction and re-entry tachyarrhythmias. This may be diagnosed by a short PR interval and a delta wave.

Treatment of tachyarrhythmias

Ventricular tachycardia

Lidocaine, amiodarone or magnesium form the mainstay of drug treatment. Overdrive pacing may be used if a pacing wire is *in situ*, capturing the ventricle at a pacing rate higher than the arrhythmia and gradually reducing the pacing rate. Torsades de pointes may be exacerbated by antiarrhythmics so magnesium or overdrive pacing are safest.

Supraventricular tachycardia and atrial flutter

Carotid sinus massage may be used in patients with no risk of calcified atheromatous carotid deposits. Amiodarone, adenosine or magnesium are usually the most useful drugs in the critically ill. Verapamil may be used if complexes are narrow (no risk of misdiagnosed ventricular tachycardia) although it and other AV node blockers should be avoided in re-entry tachycardias.

Atrial fibrillation

Acute or paroxysmal atrial fibrillation should be treated as for supraventricular tachycardia. Digoxin is more useful for chronic atrial fibrillation and does not prevent paroxysmal episodes.

Drug doses and cautions

Adenosine	3mg IV as a rapid bolus. If no response in 1min give 6mg followed by 12mg.
Verapamil	2.5mg IV slowly. If no response repeat to a maximum of 20mg. An intravenous infusion of 1–10mg may be used. 10ml CaCl 10% should be available to treat hypotension associated with verapamil. Verapamil should be avoided in re-entry tachyarrhythmias since ventricular response may increase. Life threatening hypotension may occur in misdiagnosed ventricular tachycardia and life threatening bradycardia may occur if the patient has been β-blocked.
Lidocaine	1mg/kg intravenously as a bolus followed by an infusion of 2–4mg/min.
Amiodarone	5mg/kg over 20min then infused at up to 15mg/kg/24h in 5% glucose via a central vein. Avoid with other class III agents (e.g. sotalol) since QT interval may be severely prolonged.
Magnesium	20mmol $MgSO_4$ over 2–3h. In an emergency it may be given over 5min

See also:

Defibrillation, p52; ECG monitoring, p108; Antiarrhythmics, p204; Basic resuscitation, p270; Cardiac arrest, p272; Fluid challenge, p274; Hypotension, p312; Acute coronary syndrome (1), p320; Hyperkalaemia, p420; Hypokalaemia, p422; Thyroid emergencies, p446; Tricyclic antidepressant poisoning, p460; Anaemia, p400; Pyrexia (1), p518; Pyrexia (2), p520; Pain, p532

Bradyarrhythmias

If peripheral pulses are not palpable a bradyarrhythmia requires external cardiac massage and treatment as for asystole. For asymptomatic bradycardia treatment may not be required other than close monitoring and correction of the cause. The exception to this is higher degrees of heart block occurring after an acute anterior myocardial infarction where pacing may be required prophylactically.

Causes of bradyarrhythmias

Where possible the cause of a bradyarrhythmia should be treated. Common causes for which specific treatment may be required include hypovolaemia, hypotension (may also be due to the arrhythmia), acute myocardial infarction, digoxin toxicity, β-blocker toxicity, hyperkalaemia, hypothyroidism, hypopituitarism and raised intracranial pressure. Digoxin toxicity may require treatment with antidigoxin antibodies.

Diagnosis of bradyarrhythmias

Sinus bradycardia

Slow ventricular rate with normal P waves, normal PR interval and 1:1 AV conduction.

Heart block

Normal P waves, a prolonged PR interval and 1:1 AV conduction suggest 1° heart block. In 2° heart block the ventricles fail to respond to atrial contraction intermittently. This may be associated with regular P waves and an increasing PR interval until ventricular depolarisation fails (Mobitz I or Wenkebach) or a normal PR interval with regular failed ventricular depolarisation (Mobitz II). In the latter case the AV conduction ratio may be 2:1 to 5:1. In 3° heart block there is complete AV dissociation with a slow, idioventricular rate.

Absent P wave bradycardia

Absent P waves may represent slow atrial fibrillation or sino-atrial dysfunction. In the latter case there will be a slow, idioventricular rate.

Treatment of bradyarrhythmias

Hypoxaemia must be corrected in all symptomatic bradycardias. First line drug treatment is usually atropine 0.3mg or glycopyrrolate 200µg intravenously. If the arrhythmia fails to respond, 0.6mg followed by 1.0mg atropine may be given. Failure to respond to drugs requires temporary pacing. This may be accomplished rapidly with an external system if there is haemodynamic compromise or transvenously. Other indications for temporary pacing are shown opposite. Higher degrees of heart block after an anterior myocardial infarction will usually require permanent pacing.

Indications for temporary pacing

Persistent symptomatic bradycardia

Blackouts associated with

> 3° heart block
>
> 2° heart block
>
> RBBB and left posterior hemiblock
>
> Cardiovascular collapse
>
> Inferior myocardial infarction with symptomatic 3° heart block
>
> Anterior myocardial infarction with
>
> 3° heart block
>
> RBBB and left posterior hemiblock
>
> Alternating RBBB and LBBB

See also:

Acute coronary syndrome (1)

Principles of management of the uncomplicated myocardial infarct

- Oxygen—to maintain $SaO_2 \geq 98\%$
- Good venous access
- Continuous ECG monitoring
- Adequate pain relief
- Early thrombolysis plus aspirin (heparin if using rt-PA)
- Early β blockade
- Gradual mobilisation

Complications of myocardial infarction

- Cardiopulmonary arrest
- Continuing chest pain—may be ischaemic or pericarditic in origin
- Pump failure
- Hypotension—apart from cardiogenic shock consider hypovolaemia (e.g. post-diuretics) and a thrombolysis reaction

- Tachyarrhythmias/bradyarrhythmias
- Valve dysfunction—predominantly mitral
- Pericardial tamponade (rare)
- Ventricular septal defect (unusual, often presents 2–5 days post-infarct)
- Complications of thrombolytic therapy—arrhythmias, bleeding, anaphylactoid reaction

Management of the complicated myocardial infarct

General

- Oxygen to maintain $SaO_2 \geq 98\%$
- Appropriate and prompt monitoring and investigations as indicated, e.g. echocardiogram, pulmonary artery catheter, angiography, ECG
- Early thrombolysis should still be given. rt-PA followed by heparin should be given in preference to streptokinase if invasive procedures and/or surgery are contemplated.
- Arterial or central venous cannulation should not be delayed if clinically indicated. These procedures should be performed by an experienced operator to minimise the risk of bleeding. The subclavian route should be avoided.
- Angioplasty or revascularisation surgery is beneficial if performed early. The cardiologist should be informed promptly if a patient is admitted in pump failure, continuing pain, or valvular dysfunction.

Specific

- Cardiopulmonary arrest—cardiopulmonary resuscitation
- Continuing chest pain:
- If ischaemic—IV nitrate and heparin infusions, aspirin, clopidogrel, calcium antagonist and β-blocker (unless contraindicated); consider urgent angiography.
- If pericarditic—consider non-steroidal anti-inflammatory agent
- Management of heart failure—also consider IABP
- Tachyarrhythmia—antiarrhythmics, synchronised DC cardioversion
- Bradycardias—chronotrope, consider temporary pacing
- Valve dysfunction—heart failure management; consider surgery
- Pericardial tamponade—pericardial aspiration
- Ventricular septal defect—heart failure management, consider surgery
- Thrombolysis complications

Drug dosage

Diamorphine	2.5mg IV. Repeat prn + anti-emetic
Streptokinase	1.5 million units in 100ml 0.9% saline IV over 1h
rt-PA (alteplase)	100mg IV over 90min (15mg bolus, then 50mg over 30min, then 35mg over 60min
Reteplase	10units IV + further 10units IV 30min later
Aspirin	150mg PO od
Clopidogrel	75mg
Atenolol	50mg PO od (increase to 100mg od if not hypotensive and heart rate exceeds 70bpm) or 5mg slow IV bolus
Propranolol	10–40mg PO qds (titrate to heart rate of 60bpm)
Isosorbide dinitrate	2–40mg/h IV
GTN	10–200µg/min IV or 0.5–1mg SL
Diltiazem	60mg PO tds
Nifedipine	5–10mg sublingual or PO tds
Atropine	0.3mg IV. Repeat to maximum of 2mg
Lidocaine	1mg/kg slow IV bolus then 2–4mg/min
Amiodarone	5mg/kg over 20min then infused up to 15mg/kg/day in 5% glucose via central vein (in emergency give 150–300mg in 10–20ml 5% glucose over 3min)

Key papers

Task force or Management of acute myocardial infarction of the European Society of Cardiology. Management of acute myocardial infarction in patients presenting with ST segment elevation. Eur Heart J 2003; 24:28–66

See also:

Defibrillation, p52; Temporary pacing (1), p54; Temporary pacing (2), p56; Intra-aortic balloon counterpulsation, p58; ECG monitoring, p108; Blood pressure monitoring, p110; Central venous catheter—use, p114; Central venous catheter—insertion, p116; Pulmonary artery catheter—use, p118; Pulmonary artery catheter—insertion, p120; Cardiac output—thermodilution, p122; Cardiac output—other invasive, p124; Cardiac output—non-invasive (1), p126; Cardiac output—non-invasive (2), p128; Inotropes, p196; Vasodilators, p198; Vasopressors, p200; Antiarrhythmics, p204; Chronotropes, p206; Anticoagulants, p248; Thrombolytics, p250; Basic resuscitation, p270; Cardiac arrest, p272; Fluid challenge, p274; Hypotension, p312; Tachyarrhythmias, p316; Bradyarrhythmias, p318; Acute coronary syndrome (2), p322; Heart failure—assessment, p324; Heart failure—management, p326; Pain, p532

Acute coronary syndrome (2)

Angina

Ischaemic or, rarely, spasmodic constriction of coronary arteries resulting in pain, usually precordial, pressing or crushing, and with or without radiation to jaw, neck or arms. The sedated, ventilated patient will not usually complain of pain but signs of discomfort may be apparent, e.g. sweating, hypertension, tachycardia. The ECG should be regularly scrutinised for ST segment and/or T wave changes.

Unstable angina encompasses a spectrum of syndromes between stable angina and myocardial infarction. Anginal attacks may be increased in frequency and/or severity, persist longer, respond less to nitrates, and occur at rest or after minimal exertion.

Pathophysiology

- Myocardial oxygen supply–demand imbalance usually due to coronary artery atheroma ± disruption of plaque or new non-occlusive thrombus formation. Spasm (Prinzmetal angina) is uncommon.

- Vasopressor drugs may compromise myocardial perfusion by further constricting an already stenosed vessel.

- Vasodilator drugs may also compromise myocardial perfusion by a 'coronary steal' phenomenon where blood flow is redistributed away from stenosed vessels.

Diagnosis

- Symptoms, especially chest pain but also non-specific, e.g. sweating

- ECG changes—ST segment elevation/depression, T wave inversion

- No rise in cardiac enzymes or troponin above the myocardial infarction threshold

- Dyskinetic areas of myocardium may be seen on echocardiography or angiography

Treatment

- Ensure adequate oxygenation

- Correct hypotension and tissue hypoperfusion

- Consider drug causes, e.g. vasopressors

- Glyceryl trinitrate 0.5mg SL, or nitrolingual spray (0.4–0.8mg) repeated as necessary

- If symptoms are severe and/or persisting, maintain bed rest

- Aspirin 75mg od PO (unless contraindicated).

For continuing angina:

- IV Nitrate infusion, e.g. glyceryl trinitrate, isosorbide trinitrate

- Consider calcium antagonist, e.g. diltiazem though not alone

- Consider β-blocker (unless contraindicated), e.g. propranolol, atenolol

- LMW heparin and clopidogrel (unless contraindicated)

- Consider GP2b3a inhibitor (IV eptifibatide or tirofiban) in addition to aspirin and clopidogrel if considered at high risk of MI or death

- If symptoms or ST-segment changes persist despite optimal pharmacological intervention, inform cardiologist with a view to angiography and possible angioplasty or surgery.

Key trial

Yusuf S for the Clopidogrel in Unstable Angina to Prevent Recurrent Events Trial Investigators. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. N Engl J Med. 2001; 345:494–502

Heart failure—assessment

Impaired ability of the heart to supply adequate oxygen and nutrients to meet the demands of the body's metabolising tissues.

Major causes

- Myocardial infarction/ischaemia

- Drugs e.g. β-blockers, cytotoxics

- Tachy- or bradyarrhythmias

- Valve dysfunction

- Sepsis

- Septal defect

- Cardiomyopathy/myocarditis

- Pericardial tamponade

Clinical features

Decreased forward flow leading to poor tissue perfusion

- Muscle fatigue leading ultimately to hypercapnia and collapse
- Confusion, agitation, drowsiness, coma
- Oliguria
- Increasing metabolic acidosis, arterial hypoxaemia and dyspnoea

Increased venous congestion secondary to right heart failure

- Peripheral oedema
- Hepatic congestion
- Splanchnic ischaemia
- Raised intracranial pressure

Increased pulmonary hydrostatic pressure secondary to left heart failure

- Pulmonary oedema, dyspnoea
- Hypoxaemia

Investigations

Test	Diagnosis
ECG	Myocardial ischaemia/infarction, arrhythmias
CXR	With left heart failure: pulmonary oedema (interstitial perihilar ('bat's wing') shadowing, upper lobe blood diversion, Kerley B lines, pleural effusion) ± cardiomegaly
Pulmonary artery catheter	Low cardiac output and stroke volume, low mixed venous oxygen saturation (<60%), raised PAWP (with left heart failure), raised RAP (with right heart failure). V waves with mitral or tricuspid regurgitation
Blood tests	Low SaO_2, variable $PaCO_2$, base deficit >2mmol/l, hyperlactataemia, low venous O_2 (mixed or central venous), raised cardiac enzymes, troponin, BNP, thyroid function (if indicated)
Echocardiogram	Poor myocardial contractility, pericardial effusion, valve stenosis/incompetence

Notes
Peripheral oedema implies total body salt and water retention but not necessarily intravascular fluid overload.

See also:

Heart failure—management

Basic measures

1. Determine likely cause and treat as appropriate, e.g. antiarrhythmic
2. Oxygen—to maintain $SaO_2 \geq 98\%$
3. GTN spray SL then commence IV nitrate infusion titrated rapidly until good clinical effect. Beware hypotension which, at low dosage, is suggestive of left ventricular underfilling, e.g. hypovolaemia, tamponade, mitral stenosis, pulmonary embolus

4. If patient is agitated or in pain, give diamorphine IV.

5. Consider early CPAP, BiPAP and/or IPPV to reduce work of breathing and provide good oxygenation. Cardiac output will often improve. Do not delay until the patient is *in extremis*.

6. Furosemide is rarely needed as first line therapy unless intravascular fluid overload is causative. Initial symptomatic relief is provided by its prompt vasodilating action; however, subsequent diuresis may result in marked hypovolaemia leading to compensatory vasoconstriction, increased cardiac work and worsening myocardial function. Diuretics may be indicated for acute-on-chronic failure, especially if the patient is on long term diuretic therapy but should not be used if hypovolaemic. If furosemide is required, start at low doses then reassess.

Directed management

1. Adequate monitoring (e.g. pulmonary artery catheterisation) and investigation (echocardiography).

2. If evidence exists for hypovolaemia, give 100–200ml colloid fluid challenges to achieve optimal stroke volume.

3. If vasoconstriction persists (SVR >1400dyn/s/cm^5), titrate nitrate infusion further to optimise stroke volume and, ideally, reduce SVR <1300dyn/s/cm^5. If hypovolaemia is suspected (i.e. stroke volume falls), fluid challenges should be given to re-optimise the stroke volume. Within 24h of nitrate infusion, commence ACE inhibition, initially at low dose but rapidly increased to appropriate long-term doses.

4. Inotropes are indicated if evidence of tissue hypoperfusion, hypotension or vasoconstriction persists despite optimal fluid loading and nitrate dosing. Consider epinephrine, dobutamine or milrinone; while epinephrine may sometimes cause excessive constriction, dobutamine and milrinone may excessively vasodilate. Levosimendan increases cardiac output though not at the expense of increased cardiac work.

5. Intra-aortic balloon counterpulsation augments cardiac output, reduces cardiac work and improves coronary artery perfusion.

6. Angioplasty or surgical revascularization are beneficial if performed early after myocardial infarct. Surgery may also be necessary for mechanical defects, e.g. acute mitral regurgitation.

Treatment end-points

1. BP and cardiac output adequate to maintain organ perfusion (e.g. no oliguria, confusion, dyspnoea nor metabolic acidosis). A mean BP of 60mmHg is usually sufficient but may need to be higher, especially if premorbid blood pressures are high.

2. A mixed venous oxygen saturation ≥60%. Excessive inotropes should be avoided as myocardial oxygen demand is increased.

3. Symptomatic relief.

Drug dosage

GTN	2–40mg/h IV or 0.4–0.8mg by SL spray
Isosorbide dinitrate	2–40mg/h IV
Nesiritide	2µg/kg bolus followed by infusion of 0.01–0.03µg/kg/min.
Sodium nitroprusside	20–400µg/min IV
Captopril	6.25mg PO test dose increasing to 25mg tds
Enalapril	2.5mg PO test dose increasing to 40mg od
Lisinopril	2.5mg PO test dose increasing to 40mg od
Epinephrine	Infusion starting from 0.05µg/kg/min
Dobutamine	2.5–25µg/kg/min IV
Dopamine	2.5–25µg/kg/min IV

Milrinone	Loading dose of 50µg/kg IV over 10min followed by infusion from 0.375–0.75µg/kg/min.
Enoximone	Loading dose of 0.5–1mg/kg IV over 10min followed by infusion from 5–20µg/kg/min.
Levosimendan	12–24µg/kg over 10min followed by 0.1µg/kg/min for 24h
Diamorphine	2.5mg IV. Repeat every 5min as necessary
Furosemide	10–20mg IV bolus. Repeat or increase as necessary

Key trials

Cotter G, et al. Randomised trial of high-dose isosorbide dinitrate plus low-dose furosemide versus high-dose furosemide plus low-dose isosorbide dinitrate in severe pulmonary oedema. Lancet 1998; 351:389–93

Cuffe MS, et al. Rationale and design of the OPTIME CHF trial: outcomes of a prospective trial of intravenous milrinone for exacerbations of chronic heart failure. Am Heart J 2000; 139:15–22

Follath F, et al. Efficacy and safety of intravenous levosimendan compared with dobutamine in severe low-output heart failure (the LIDO study): a randomised double-blind trial. Lancet 2002; 360:196–202

See also:

Ovid: Oxford Handbook of Critical Care

Renal Disorders

Oliguria

Defined as a urine output <0.5ml/kg/h and caused by:

- Post-renal—urinary tract obstruction, e.g. blocked catheter, ureteric trauma, prostatism, raised intra-abdominal pressure, blood clot, bladder tumour.
- Renal—established acute renal failure, acute tubular necrosis, glomerulonephritis.
- Pre-renal—hypovolaemia, low cardiac output, hypotension, inadequate renal blood flow.

Obstruction and pre-renal causes of oliguria must be excluded before resorting to diuretics.

Urinary tract obstruction

A full bladder should be excluded by palpation. Ensure a patent catheter is present. If obstruction is due to blood clot the bladder should be irrigated. If obstruction is suspected higher in the renal tract an ultrasound scan is required for diagnosis and possible urological intervention (e.g. nephrostomies). Raised intra-abdominal pressure may cause oliguria by impeding renal venous drainage (particularly if >20mmHg). Relief of the high pressure often promotes a diuresis.

Hypovolaemia

Once renal tract obstruction is excluded, it is mandatory to correct hypovolaemia by fluid challenge. Oliguria in hypovolaemic patients may be a physiological response or due to a reduced renal blood flow.

Inadequate renal blood flow and/or pressure

If cardiac output remains low despite correction of hypovolaemia, correction with vasodilators and/or inotropes will be necessary. If the blood pressure remains low after improving the cardiac output, vasopressors may be needed to achieve a mean blood pressure of at least 60mmHg. In elderly patients and others with pre-existing hypertension, a

higher mean blood pressure may be necessary to maintain urine output.

Persistent oliguria

Attempts to increase urine output with diuretics may follow the above measures if oliguria persists. Furosemide is given in a dose of 5–10mg intravenously with higher increments at 30min intervals to a maximum of 250mg. Higher doses may be needed if the patient has previously received diuretic therapy. A low dose infusion may be started (1–5mg/h IV). Mannitol (20g intravenously) may be considered although failure to promote a diuresis may increase oedema formation. Failure to re-establish urine output may require renal support in the form of dialysis or haemofiltration. There is no point in continuing diuretic therapy if it is not effective; loop diuretics in particular may be nephrotoxic. Indications for renal support include fluid overload, hyperkalaemia, metabolic acidosis, creation of space for nutrition or drugs, persistent renal failure with rising urea and creatinine, and symptomatic uraemia.

Biochemical assessment

	Pre-renal cause	Renal cause
Urine osmolality (mOsmol/kg)	>500	<400
Urine Na (mmol/l)	<20	>40
Urine:Plasma creatinine	>40	<20
Fractional Na excretion*	<1	>2

* $\dfrac{100 \times Urine:Plasma\ [Na^+]}{Urine:Plasma\ [Creatinine]}$

See also:

Haemo(dia)filtration (1), p62; Haemo(dia)filtration (2), p64; Peritoneal dialysis, p66; Blood pressure monitoring, p110; Urea & creatinine, p144; Urinalysis, p166; Colloid osmotic pressure, p172; Crystalloids, p176; Colloids, p180; Diuretics, p212; Dopamine, p214; Basic resuscitation, p270; Fluid challenge, p274; Hypotension, p312; Acute renal failure—diagnosis, p332; Acute renal failure—management, p334; Bowel perforation and obstruction, p348; Abdominal sepsis, p350; Pancreatitis, p354; Acute liver failure, p360; Hyperkalaemia, p420; Sepsis and septic shock—treatment, p486; Malaria, p490; Multiple trauma (1), p500; Multiple trauma (2), p502; Burns—fluid management, p510; Rhabdomyolysis, p528; Post-operative intensive care, p534

Acute renal failure—diagnosis

Renal failure is defined as renal function inadequate to clear the waste products of metabolism despite the absence of or correction of haemodynamic or mechanical causes. Renal failure is suggested by:

- Uraemic symptoms (drowsiness, nausea, hiccough, twitching)
- Raised plasma creatinine (>200µmol/l)
- Hyperkalaemia
- Hyponatraemia
- Metabolic acidosis

Persistent oliguria may be a feature of acute renal failure but non-oliguric renal failure is not uncommon; 2–3l of poor quality urine per day may occur despite an inadequate glomerular filtration rate. The prognosis is better if urine output is maintained. Clinical features may suggest the cause of renal failure and dictate further investigation. Acute tubular necrosis is a common aetiology in the critically ill (e.g. following hypovolaemia, extensive burns) but other causes must be borne in mind. In sepsis, the kidney often has a normal histological appearance. Anaemia implies chronic renal failure.

Post-operative renal failure

Risk factors include hypovolaemia, haemodynamic instability (particularly hypotension), major abdominal surgery in those >50 years, major surgery in jaundiced patients and biliary and other sepsis. Surgical procedures (particularly gynaecological) may be complicated by damage to the lower urinary tract with an obstructive nephropathy. Abdominal aortic aneurysm surgery may be associated with renal arterial disruption and should be investigated urgently with renography and possible arteriography or re-exploration.

Other causes

- Nephrotoxins—may cause renal failure via acute tubular necrosis, interstitial nephritis or renal tubular obstruction. All potential nephrotoxins should be withdrawn.

- Rhabdomyolysis—suggested by myoglobinuria and raised CPK in patients who have suffered a crush injury, coma or seizures.

- Glomerular disease—red cell casts, haematuria, proteinuria and systemic features (e.g. hypertension, purpura, arthralgia, vasculitis) are all suggestive of glomerular disease. Renal biopsy or specific blood tests (e.g. Goodpasture's syndrome, vasculitis) are required to confirm diagnosis and appropriate treatment.

- Haemolytic uraemic syndrome—suggested by haemolysis, uraemia, thrombocytopenia and neurological abnormalities.

- Crystal nephropathy—suggested by the presence of crystals in the urinary sediment. Microscopic examination of the crystals confirms the diagnosis (e.g. urate, oxalate). Release of purines and urate are responsible for acute renal failure in the tumour lysis syndrome.

- Renovascular disorders—loss of vascular supply may be diagnosed by renography. Complete loss of arterial supply may occur in abdominal trauma or aortic disease (particularly dissection). More commonly, the arterial supply is partially compromised (e.g. renal artery stenosis) and blood flow is further reduced by haemodynamic instability or locally via drug therapy (e.g. NSAIDs, ACE inhibitors). Renal vein obstruction may be due to thrombosis or external compression (e.g. raised intra-abdominal pressure).

Nephrotoxins

The following are some common nephrotoxins:

Allopurinol	Aminoglycosides
Amphotericin	Cephalosporins
Dextran 40	Furosemide
Heavy metals	Herbal medicines
Narcotics	NSAIDs
Organic solvents	Paraquat
Penicillins	Pentamidine
Phenytoin	Radiographic contrast
Sulphonamides	Tetracyclines
Thiazides	Vancomycin

See also:

Acute renal failure—management

Identification and correction of reversible causes of renal failure is crucial. All cases require careful attention to fluid management and nutritional support. Dialysis and/or filtration techniques will make space for adequate fluid and nutritional intake.

Urinary tract obstruction

Lower tract obstruction requires the insertion of a catheter (suprapubic if there is urethral disruption) to allow tract decompression. Ureteric obstruction requires urinary tract decompression by nephrostomy or stent. A massive diuresis is common after decompression so it is important to ensure adequate circulating volume to prevent secondary pre-renal failure.

Haemodynamic management

Pre-renal failure is reversible before it becomes established. Careful fluid management to ensure an adequate circulating volume and any necessary inotrope or vasopressor support may establish a diuresis. If oliguria persists after pre-renal factors have been corrected, the use of diuretics (furosemide, mannitol) may establish a diuresis.

Metabolic management

Hyperkalaemia may be life-threatening (>6.5mmol/l or ECG changes) and may be prevented by potassium restriction, early dialysis or haemo(dia)filtration. Hypocalcaemia and hyponatraemia are best treated with dialysis and/or haemo(dia)filtration, although calcium supplementation may be used. Hyponatraemia is usually due to water excess although salt-losing nephropathies (acute tubular necrosis, other renal tubular disorders) may require sodium chloride supplements. Hyperphosphataemia may be treated with dialysis, filtration or aluminium hydroxide orally. Metabolic acidosis (not due to tissue hypoperfusion) may be corrected with dialysis, filtration or 1.26% sodium bicarbonate infusion.

Nephrotoxins and crystal nephropathies

All nephrotoxic agents should be withheld if possible. All necessary drugs should have their dosage modified according to the GFR. In some cases urinary excretion of nephrotoxins and crystals may be encouraged by urinary alkalinisation to maintain their solubility with an induced diuresis (rhabdomyolysis, acidic crystals). Dialysis may also be useful.

Glomerular disease

Immunosuppressive therapy may be useful after diagnosis has been confirmed. Dialysis is often required for the more severe forms of glomerulonephritis despite steroid responsiveness.

Urgent treatment of hyperkalaemia

- 10–20ml calcium chloride 10% by slow intravenous injection.
- 100ml 8.4% sodium bicarbonate intravenously.
- Glucose (50g) and insulin (10–20IU) intravenously with careful blood glucose monitoring and urgent haemodialysis.

Renal replacement therapy

Continuous haemofiltration forms the mainstay of replacement therapy in critically ill patients who often cannot tolerate haemodialysis due to haemodynamic instability. Peritoneal dialysis is not commonly used today. Acute renal failure in the critically ill usually recovers within 1–6 weeks; permanent renal failure is rare.

General indications for dialysis or haemo(dia)filtration

Fluid excess (e.g. pulmonary oedema)

Hyperkalaemia (>6.0mmol/l)

Metabolic acidosis (pH <7.2) due to renal failure

Clearance of dialysable nephrotoxins and other drugs

Creatinine rising >100µmol/l/day

Creatinine >300–600µmol/l

Urea rising >16–20mmol/l/day

To create space for nutrition or drugs

See also:

Haemo(dia)filtration (1), p62; Haemo(dia)filtration (2), p64; Peritoneal dialysis, p66; Crystalloids, p176; Colloids, p180; Diuretics, p212; Dopamine, p214; Basic resuscitation, p270; Fluid challenge, p274; Oliguria, p330; Acute renal failure—diagnosis, p332; Hyperkalaemia, p420; Hyponatraemia, p418; Hypocalcaemia, p428; Metabolic acidosis, p434

Gastrointestinal Disorders

Vomiting/gastric stasis

While vomiting *per se* is relatively rare in the ICU patient, large volume gastric aspirates are commonplace and probably represent the major reason for failure of enteral nutrition.

Ileus

Ileus affects the stomach more frequently than the rest of the gastrointestinal tract. Abdominal surgery, drugs (particularly opiates), gut dysfunction as a component of multi-organ dysfunction, hypoperfusion and prolonged starvation may all contribute to gastric ileus. Early and continued use of the bowel for feeding appears to maintain forward propulsive action. Management consists of treating the cause where possible, the use of motility stimulants such as metoclopramide or erythromycin and, in resistant cases, bypassing the stomach with a nasoduodenal/nasojejunal tube or a jejunostomy.

Upper bowel obstruction

Relatively unusual; apart from primary surgical causes such as neoplasm or adhesions, the predominant cause in the ICU is gastric outlet obstruction. This may be related to long-standing peptic ulcer disease or may occur in the short term from pyloric and/or duodenal swelling consequent to gastritis or duodenitis. This can be diagnosed endoscopically and treated by bowel rest plus an H_2 antagonist, proton pump inhibitor or sucralfate.

Gastric irritation

Drugs or chemicals—either accidental or adverse reaction (e.g. steroids, aspirin), intentional (e.g. alcohol, bleach) or therapeutic (e.g. ipecacuanaha syrup) may induce vomiting. Treatment, where appropriate, may comprise (i) removal of the cause, (ii) dilution with copious amounts of fluid (iii) neutralisation with alkali and/or H_2 antagonist or proton pump inhibitor and (iv) administration of anti-emetic (e.g. metoclopramide).

Neurological

Stimulation of the emetic centre may follow any neurological event (e.g. trauma, CVA), drug therapy (e.g. chemotherapy), pain and metabolic disturbances. Management is by treating the cause where possible and by judicious use of anti-emetics, initially metoclopramide or prochlorperazine. Consider ondansetron or granisetron if these are unsuccessful.

See also:

Enteral nutrition, p80; Electrolytes

$(Na^+, K^+, Cl^-, HCO_3^-)$

, p146; Opioid analgesics, p234; Anti-emetics, p224; Gut motility agents, p226; Bowel perforation and obstruction, p348; Electrolyte management, p414; Poisoning—general principles

Diarrhoea

The definition of diarrhoea in the ICU patient is problematic as the amount of stool passed daily is difficult to measure. Frequency and consistency may also vary significantly. Loose/watery and frequent ($\geq 4 \times$ day) stool will often require investigation and/or treatment.

Commoner ICU causes

- Infection—*Clostridium difficile*, gastroenteritis (e.g. *Salmonella, Shigella*), rarer tropical causes (e.g. cholera, dysentry, giardiasis, tropical sprue).

- Drugs, e.g. antibiotics, laxatives.

- Gastrointestinal—feed (e.g. lactose intolerance), coeliac disease, other malabsorption syndromes, inflammatory bowel disease, diverticulitis, pelvic abscess, bowel obstruction with overflow. Enteral feed is often implicated but rarely causative.

- For bloody diarrhoea consider infection, ischaemic or inflammatory bowel disease.

Diagnosis

- Rectal examination to rule out impaction with overflow. Consider sigmoidoscopy if colitis or *C. difficile* suspected (pseudomembrane seen).

- Stool sent to laboratory for MC & S, *C. difficile* toxin.

- Fat estimation (malabsorption) is rarely necessary in the ICU patient

- If ischaemic or inflammatory bowel disease suspected, perform a supine abdominal X-ray and inspect for dilated loops of bowel (NB toxic megacolon), thickened walls (increased separation between loops) and 'thumbprinting' (suggestive of mucosal oedema). Fluid levels seen on erect or lateral abdominal X-ray may be seen in diarrhoea or paralytic ileus and do not necessarily indicate obstruction. Diarrhoea is often but not always bloody.

- If abscess suspected, perform ultrasonography or CT scan

Management

1. Treat cause where possible e.g. for *C. difficile*, metronidazole plus cholesytramine (binds the toxin).

2. Consider temporary (12–24h) cessation of enteral feed if very severe. Consider change in feed if appropriate, e.g. coeliac disease, lactose intolerance.

3. Consider stopping antibiotics.

4. Give antidiarrhoeal if infection excluded.

5. Careful attention to fluid and electrolyte balance (in particular Na^+, K^+, Mg^{2+}).

6. Request surgical opinion if infarcted or inflamed bowel or abscess suspected.

See also:

Failure to open bowels

Commoner ICU causes

- Prolonged ileus/decreased gut motility (e.g. opiates, post-surgery)

- Lack of enteral nutrition

- Bowel obstruction—this is a relatively uncommon secondary event and is mainly seen post-operatively, either after a curative procedure or with development of adhesions

Management

1. Clinically exclude obstruction and confirm presence of stool per rectum.

2. Ensure adequate hydration.

3. Anticonstipation therapy may be given, usually starting with laxatives (e.g. lactulose or, for more urgent response, magnesium sulphate), then proceeding to glycerine suppositories and, finally, enemata if gentler measures prove unsuccessful.

4. Consider reducing/stopping dose of opiate if possible.

See also:

Upper gastrointestinal haemorrhage

Causes

- Peptic ulceration

- Oesophagitis/gastritis/duodenitis

- Varices

- Mallory–Weiss lower oesophageal tear

- Neoplasms

Pathophysiology
Peptic ulceration is related to protective barrier loss leading to acid or biliary damage of the underlying mucosa and submucosa. Barrier loss occurs secondary to critical illness, alcohol, drugs, e.g. non-steroidals, poisons including corrosives. Direct damage, especially at the lower oesophagus, may occur from feeding tubes. Mucosal damage ('stress ulcers') may also occur as a consequence of tissue hypoperfusion. Gastric hypersecretion is uncommon in critically ill patients; indeed, gastric acid content and secretion is often reduced.

Prophylaxis

- Small-bore feeding tubes

- Nasogastric enteral nutrition (nasojejunal and parenteral feeding has also been shown to reduce the incidence of

stress ulcer bleeding)

- Adequate tissue perfusion (flow and pressure)

- The role of prophylactic drug therapy including H$_2$ antagonists, proton pump inhibitors and sucralfate is controversial. Evidence suggests that enteral nutrition alone is as effective and there are claims that loss of the acid environment in the stomach predisposes the patient to nosocomial infection. Patients at highest risk are those requiring prolonged mechanical ventilation or with a concurrent coagulopathy.

Treatment of major haemorrhage

- Fluid resuscitation with colloid and blood with blood products as appropriate to correct any coagulopathy. Maintain haemoglobin between 7–10g/dl and have adequate cross-matched blood available should further large haemorrhages occur.

- If possible, discontinue any on-going anticoagulation, e.g. heparin.

- Urgent diagnostic fibreoptic endoscopy. Local injection of epinephrine or a sclerosant into (or thermal sealing of) a bleeding peptic ulcer base may halt further bleeding. Likewise, banding or sclerosant injection may arrest bleeding varices.

- If oesophageal varices are known or highly suspected, consider vasopressin or terlipressin ± a Sengstaken-type tube for severe haemorrhage, either as a bridge to endoscopy or if banding/injection is unsuccessful. Remember that sources of bleeding other than varices may be present, e.g. peptic ulcer.

- For peptic ulceration and generalised inflammation commence an H$_2$ antagonist or proton pump inhibitor. Give intravenously to ensure effect. Enteral antacid may also be beneficial.

- Surgery is rarely necessary but should be considered if bleeding continues, e.g. >6–10 unit transfusion requirement. Inform a surgeon promptly of any patient with major bleeding.

See also:

Bleeding varices

Varices develop following a prolonged period of portal hypertension, usually related to liver cirrhosis. Approximately one third will bleed. They are commonly found in the lower oesophagus but, occasionally, in the stomach or duodenum. Torrential haemorrhage may occur. Approximately 50% of patients die within 6 weeks of presentation of their first bleed; each subsequent bleed carries a 30% mortality.

Management

1. If airway and/or breathing are compromised, perform endotracheal intubation and institute mechanical ventilation. This facilitates Sengstaken-type tube placement and endoscopy but may be associated with severe hypotension secondary to covert hypovolaemia. If possible, ensure adequate intravascular filling before intubation.

2. Fluid resuscitation with colloid and blood with blood products as appropriate to correct any coagulopathy. Ensure good venous access (at least two 14G cannulae). Group-specific or O-negative blood may be needed for emergency use. Maintain haemoglobin >10g/dl and have at least 4 units of cross-matched blood available for urgent transfusion. There is a theoretical risk that over-transfusion may precipitate further bleeding by raising portal venous pressure. Cardiac output monitoring should be considered if the patient remains haemodynamically unstable or there is a history of heart disease.

3. If bleeding is torrential, insert a Sengstaken-type tube and commence administration of IV vasopressin/terlipressin (*q.v.*).

4. Gentle placement of a large-bore nasogastric tube is a reasonably safe procedure that facilitates drainage of blood, lessens the risk of aspiration and can be used to assess continuing blood loss.

5. Perform urgent fibreoptic endoscopy to exclude other sources of bleeding. This also permits variceal banding or local injection of a sclerosing agent. Bleeding is arrested in up to 90% of cases. Endoscopy may be impossible in the short term if bleeding is too severe. It may have to be delayed for 6–24h until a period of tamponade by the Sengstaken-type tube ± vasopressin has enabled some control of the bleeding.

6. Either octreotide, vasopressin or terlipressin can be administered for severe bleeding, or prophylaxis against fresh bleeding. Vasopressin controls bleeding in approximately 60% of cases and its efficacy and safety appears to be enhanced by concurrent GTN. The side-effect profile of terlipressin is lower as it does not appear to precipitate as much mesenteric, cardiac or digital ischaemia, Octreotide is a somatostatin analogue but longer-acting than its parent compound; like somatostatin, it is probably as effective as vasopressin but without

the side-effects.

7. If bleeding continues after prolonged balloon tamponade (2–3 days) and repeated endoscopy, consider transjugular intrahepatic portosystemic stented shunt (TIPSS). This can be performed quickly and carries a relatively low mortality compared to surgery although the risk of encephalopathy is increased.

8. The traditional alternative to TIPSS is oesophageal transection (now performed with a staple gun) with or without devascularisation. Mortality in the acute situation is of the order of 30%.

Drug dosages

Octreotide	50µg bolus then 50µg/h infusion
Vasopressin	20 units over 20min then 0.4 units/min infusion
	Also give glyceryl trinitrate 2–20mg/h to counteract myocardial and mesenteric ischaemia
Terlipressin	2mg IV followed by 1–2mg IV 4–6-hrly until bleeding controlled for up to 72h

See also:

Bowel perforation and obstruction

Patients with bowel perforation or obstruction may be admitted to the ICU after surgery, for pre-operative resuscitation and cardiorespiratory optimisation, or for conservative management. Although rarely occurring *de novo* in the ICU patient, these conditions may be difficult to diagnose because of sedation ± muscle relaxation. Consider when there is:

- Abdominal pain, tenderness, peritonism
- Abdominal distension
- Agitation
- Increased nasogastric aspirates, vomiting
- Increasing metabolic acidosis
- Signs of hypovolaemia or sepsis

A firm diagnosis is often not made until laparotomy although supine and either erect or lateral abdominal X-ray may reveal either free gas in the peritoneum (perforation) or dilated bowel loops with multiple fluid levels (obstruction). Ultrasound is usually unhelpful though faecal fluid may occasionally be aspirated from the peritoneum following perforation.

It may be difficult to distinguish bowel obstruction from a paralytic ileus as (i) bowel sounds may be present or absent in either and (ii) X-ray appearances may be similar.

Management

1. Correct fluid and electrolyte abnormalities. Resuscitation should be prompt and aggressive and usually consists of colloid replacement plus blood to maintain Hb >7g/dl. Inotropes or vasopressors may be required to restore an adequate circulation, particularly following perforation. Early cardiac output monitoring should be considered if the circulatory status remains unstable or vasoactive drugs are required.

2. The surgeon should be informed early. A conservative approach may be adopted, e.g. with upper small bowel perforation; however, surgery is usually required for large bowel perforation. Small or large bowel obstruction may sometimes be managed conservatively as spontaneous resolution may occur, e.g. adhesions. Prompt exploration should be encouraged if the patient shows signs of systemic toxicity.

3. Both conservative and post-operative management of perforation and obstruction usually require continuous nasogastric drainage to decompress the stomach, nil by mouth and parenteral nutrition.

4. Pain relief should not be withheld.

5. Broad spectrum antibiotic therapy should be commenced for bowel perforation after appropriate specimens have been taken for laboratory analysis. Therapy usually comprises aerobic and anaerobic Gram negative cover (e.g. 2nd or 3rd generation cephalosporin, quinolone or carbapenem, plus metronidazole ± aminoglycoside).

6. Post-operative management of bowel perforation may involve repeated laparotomies to exclude collections of pus and bowel ischaemia/infarction; surgery should be expedited if the patient's condition deteriorates. Alternatively, regular imaging ± drainage of collections may be needed.

See also:

Parenteral nutrition, p82; Failure to open bowels, p342; Abdominal sepsis, p350; Pancreatitis, p354; Metabolic acidosis, p434; Systemic inflammation/multiorgan failure, p484; Post-operative intensive care, p534

Lower intestinal bleeding and colitis

Causes of lower gastrointestinal bleeding

- Bowel ischaemia/infarction
- Inflammatory bowel disease (ulcerative colitis, Crohn's disease)
- Infection, e.g. *Shigella, Campylobacter*, amoebic dysentry
- Upper gastrointestinal source, e.g. peptic ulceration
- Angiodysplasia
- Neoplasm

Although relatively rare, massive lower gastrointestinal haemorrhage can be life-threatening.

Ischaemic/infarcted bowel

Can occur following prolonged hypoperfusion or, occasionally, secondary to a mesenteric embolus. It usually presents with severe abdominal pain, bloody diarrhoea and signs of systemic toxicity including a rapidly increasing metabolic acidosis. Plasma phosphate levels may also be elevated. X-ray appearances of thickened, oedematous bowel loops ('thumb printing') with an increased distance between bowel loops are suggestive. Treatment is by restoration of tissue perfusion, blood transfusion to maintain haemoglobin >7g/dl and, if clinical features fail to settle promptly, laparotomy with a view to bowel excision.

Inflammatory bowel disease

Presents with weight loss, abdominal pain and diarrhoea which usually contains blood. Complications of ulcerative colitis include perforation and toxic megacolon while complications of Crohn's disease include fistulae, abscesses and perforations.

Management involves:

1. Fluid and electrolyte replacement.
2. Blood transfusion to maintain haemoglobin >7g/dl.
3. High dose steroids IV and, if distal bowel involvement, by enema.
4. Nutrition (often parenteral).
5. Regular surgical review. Surgery may be indicated if symptoms fail to settle after 5–7 days, for toxic megacolon, perforation, abscesses or obstruction.
6. Antidiarrhoeal drugs should be avoided.

Angiodysplasia

Usually presents as fresh bleeding per rectum and this may be considerable. It is due to an arteriovenous malformation and commoner in the elderly. Localisation and embolisation by angiography may be curative during active bleeding, Surgery may be required if bleeding fails to settle on conservative management and, occasionally, 'blind' laparoscopic embolisation of a mesenteric vessel. However, localisation of the lesion may be difficult at laparotomy, necessitating extensive bowel resection.

See also:

Colloids, p180; Blood transfusion, p182; Coagulants and antifibrinolytics, p254; Basic resuscitation, p270; Fluid challenge, p274; Bowel perforation and obstruction, p348; Bleeding disorders, p396

Abdominal sepsis

This is a common but difficult to diagnose condition in intensive care patients. A proportion of such patients are admitted following laparotomy but others may develop abdominal sepsis *de novo* or as a secondary complication following abdominal surgery, in particular after bowel resection. Sepsis may either be localised to an organ, e.g. cholecystitis, or the peritoneal cavity (abscess); alternatively, there may be a generalised peritonitis. Non-bowel

infection or inflammation can present in a similar manner, e.g. pancreatitis, cholecystitis, gynaecological infection, pyelonephritis.

Clinical features

- Non-specific signs including pyrexia (especially swinging), neutrophilia, falling platelet count, increasing metabolic acidosis, circulatory instability
- Abdominal distension ± localised discomfort, peritonism
- Abdominal mass, e.g. gall bladder, pseudocyst, abscess
- Failure to tolerate enteral feed/large nasogastric aspirates
- Pleural effusion (if subdiaphragmatic sepsis)
- Diarrhoea (if pelvic sepsis)

Diagnosis

- Ultrasound
- CT scan
- Laparotomy
- Gallium white cell scans are occasionally useful for identification of abscesses.

Samples should be taken for microbiological analysis from blood, urine, stool, abdominal drain fluid and vaginal discharge if present. A sample of pus is preferred to a swab. Hyperamylasaemia may suggest pancreatitis though amylase levels can also be elevated with other intra-abdominal pathologies.

Treatment

- Antibiotic therapy providing Gram negative and anaerobic cover (e.g. 2nd or 3rd generation cephalosporin, quinolone or carbapenem, plus metronidazole ± aminoglycoside). Treatment can be amended depending on culture results and patient response.
- Ultrasonic or CT-guided drainage of pus.
- Laparotomy with removal of pus, peritoneal lavage, etc.

A negative laparotomy should be viewed as a useful means of excluding intra-abdominal sepsis rather than an unnecessary procedure. Laparotomy should be encouraged if the patient deteriorates and a high suspicion of abdominal pathology persists.

Cholecystitis, with or without (acalculous) gallstones, may present with signs of infection. There is a characteristic ultrasound appearance of an enlarged organ with a thickened, oedematous wall surrounded by fluid. Treatment is often conservative with antibiotics (as above) and percutaneous, ultrasound-guided drainage via a pigtail catheter. Cholecystectomy is rarely necessary in the acute situation unless the gall bladder has perforated, though some authorities argue that this is the treatment of choice for acalculous cholecystitis.

See also:

Pancreatitis

Inflammation of the pancreas and surrounding retroperitoneal tissues. The appearance of the pancreas may range from mildly oedematous to haemorrhagic and necrotising. A pseudocyst may develop which can become infected and the bile duct may be obstructed causing biliary obstruction and jaundice. Though mortality is quoted at 5–10%, this is much higher (approx. 40%) in those with severe pancreatitis requiring intensive care.

Causes

- Alcohol
- Gallstones
- Miscellaneous, e.g. ischaemia, trauma, viral, hyperlipidaemia
- Part of the multiple organ failure syndrome

Diagnosis

- Non-specific features include central, severe abdominal pain, pyrexia, haemodynamic instability, vomiting, ileus. Discolouration around the umbilicus (Cullen's sign) or flanks (Grey Turner's sign) is rarely seen.
- Plasma enzymes—elevated levels of amylase (usually >1000IU/ml) and pancreatic lipase are suggestive but non-specific. Levels may be normal, even in severe pancreatitis.
- Ultrasound
- CT scan
- Laparotomy

Complications

- Multi-organ dysfunction syndrome
- Infection/abscess formation
- Hypocalcaemia
- Diabetes mellitus
- Bleeding

Management

- General measures including fluid resuscitation, maintaining Hb at 7–10g/dl, respiratory support, analgesia, and anti-emetics. Routine antibiotic therapy is of unproved benefit.
- Adequate monitoring should be instituted, including cardiac output monitoring if cardiorespiratory instability is present.
- The patient is conventionally kept nil by mouth with continuous NG drainage, and nutrition and vitamins provided IV. However, recent studies show safety and efficacy of distal nasojejunal—and even nasogastric—enteral feeding.
- Gallstone obstruction should be relieved either endoscopically or surgically.
- Hypocalcaemia, if symptomatic, should be treated by intermittent slow IV injection (or, occasionally, infusion) of 10% calcium chloride.
- Hyperglycaemia should be controlled by a continuous insulin infusion.
- No specific treatment is routinely used.
- The role and extent of surgery remains controversial; Some advocate percutaneous drainage of infected and/or necrotic debris while surgery frequently consists of regular (often daily) laparotomy with debridement of necrotic tissue and peritoneal lavage. Pseudocysts may resolve or require drainage either percutaneously or into the bowel.

Ranson's signs of severity in acute pancreatitis

On hospital admission:

- Age >55 years old
- Blood glucose >11mmol/l
- Serum lactate dehydrogenase (LDH) >300U/l
- Serum aspartate aminotransferase (AST) >250U/l
- White blood count >16×10^9/l

At 48 h after admission:

- Haematocrit fall >10%
- Blood urea nitrogen rise >1mmol/l
- Serum calcium <2mmol/l
- PaO_2 <8kPa
- Arterial base deficit >4mmol/l
- Estimated fluid sequestration >6000ml

Pancreatitis severe if more than 2 criteria met within 48h of admission

Imrie scoring system

White blood count >15 × 10^9/l

Blood glucose >10mmol/l

Blood urea nitrogen >16mmol/l

LDH >600IU/l

AST >200IU/l

Albumin <32g/dl

Plasma calcium <2mmol/l

PaO$_2$ <8kPa

Pancreatitis severe if more than 2 criteria met within 48h of admission

APACHE II scoring system
Pancreatitis severe if APACHE *II score>8*

See also:
Ventilatory support—indications, p4; Enteral nutrition, p80; Parenteral nutrition, p82; Basic resuscitation, p270; Fluid challenge, p274; Respiratory failure, p282; Acute respiratory distress syndrome (1), p292; Acute respiratory distress syndrome (2), p294; Hypotension, p312; Oliguria, p330; Abdominal sepsis, p350; Metabolic acidosis, p434; Systemic inflammation/multiorgan failure, p484; Sepsis and septic shock—treatment, p486; Pain, p532

Hepatic Disorders

Jaundice
Jaundice is a clinical diagnosis of yellow pigmentation of sclera and skin resulting from a raised plasma bilirubin. It is usually visible when the plasma bilirubin exceeds 30–40µmol/l.

Commoner causes seen in the ICU

- Pre-hepatic—intravascular haemolysis (e.g. drugs, malaria, haemolytic uraemic syndrome), Gilbert's syndrome.

- Hepatocellular—critical illness, viral (hepatitis A, B, C, Epstein–Barr), alcohol, drugs (e.g. paracetamol, halothane), toxoplasmosis, leptospirosis.

- Cholestatic—critical illness, intrahepatic causes (e.g. drugs such as chlorpromazine, erythromycin and isoniazid, primary biliary cirrhosis), extrahepatic causes (e.g. biliary obstruction by gallstones, neoplasm, pancreatitis).

Diagnosis

- Urinalysis—unconjugated bilirubin does not appear in the urine.

- Measurement of conjugated and unconjugated bilirubin—conjugated bilirubin predominates in cholestatic jaundice, unconjugated bilirubin in pre-hepatic jaundice, and a mixed picture is often seen in hepatocellular jaundice.

- Plasma alkaline phosphatase is usually markedly elevated in obstructive jaundice while prothrombin times, aspartate transaminase and alanine aminotransferase are elevated in hepatocellular jaundice.

- Ultrasound or CT scan will diagnose extrahepatic biliary obstruction.

Management

1. Identify and treat cause. Where possible, discontinue any drug that could be implicated. If extrahepatic, consider percutaneous transhepatic drainage, bile duct stenting or, rarely, surgery.

2. Liver biopsy is rarely necessary in a jaundiced ICU patient unless the diagnosis is unknown and the possibility exists of liver involvement in the underlying pathology, e.g. malignancy.

3. Non-obstructive jaundice usually settles with conservative management as the patient recovers.

4. An antihistamine and topical calamine lotion may provide symptomatic relief for pruritus if troublesome. Cholestyramine 4g tds PO may be helpful in obstructive jaundice.

Acute liver failure

This condition results from massive necrosis of liver cells leading to severe liver dysfunction and encephalopathy. Survival rates for liver failure with Grade 3 or 4 hepatic encephalopathy vary from 10–40% on medical therapy alone, to 60–80% with orthotopic liver transplantation.

Major causes

- Alcohol

- Drugs, particularly paracetamol overdose

- Viral hepatitis, particularly hepatitis B, hepatitis C

- Poisons, e.g. carbon tetrachloride

- Acute decompensation of chronic disease, e.g. following infection

Diagnosis

- Should be considered in any patient presenting with jaundice, generalised bleeding, encephalopathy or marked hypoglycaemia.

- Abnormal liver function tests, in particular, prolonged PT or INR and hyperbilirubinaemia. In severe liver failure, plasma enzyme levels may not be elevated.

Management

- General measures include fluid resuscitation and blood transfusion to keep Hb 7–10g/dl. The circulation is usually hyperdynamic and dilated; vasopressors may be needed to maintain an adequate BP.

- Correction of coagulopathy is often withheld as this provides a good guide to recovery or the need for transplantation. Use of fresh frozen plasma is restricted to patients who are bleeding or are about to undergo an invasive procedure.

- Adequate monitoring should be instituted if cardiorespiratory instability is present.

- Mechanical ventilation may be necessary if the airway is unprotected or respiratory failure develops. Lung shunts are frequently present, causing hypoxaemia.

- Infection is commonplace and is frequently either Gram positive or fungal. Clinical signs are often absent. Samples of blood, sputum, urine, wound sites, drain fluid, intravascular catheter sites and ascites should be sent for regular microbiological surveillance. Systemic antimicrobial therapy, with or without selective gut decontamination, has been shown to reduce the infection rate. Fungal infections are also well recognised. Some Liver Units give prophylactic antifungal therapy.

- Hypoglycaemia is a common occurrence. It should be frequently monitored and treated with either enteral (or parenteral) nutrition, or a 10–20% glucose infusion to maintain normoglycaemia.

- Renal failure occurs in 30–70% of cases and may necessitate renal replacement therapy. The incidence may be reduced by careful maintenance of intravascular volume. Vasopressin/terlipressin has also been used successfully for hepatorenal syndrome.

- Upper gastrointestinal bleeding is more common due to the associated coagulopathy. Prophylactic H_2 blockers or proton pump inhibitors may be of benefit.

- *N*-acetylcysteine and/or epoprostenol improves O_2 consumption. Though tissue hypoxia may be reduced by these drugs, particularly when vasopressor drugs are needed, outcome benefit remains unproved.

- Corticosteroids, prostaglandin E and charcoal haemoperfusion have not been shown to have any outcome benefit.

Hepatic encephalopathy

Grading

1. Confused, altered mood

2. Inappropriate, drowsy

3. Stuporose but rousable, very confused, agitated

4. Coma, unresponsive to painful stimuli

The risk of cerebral oedema is far higher at Grades 3 and 4 (50–85%) and is the leading cause of death. Suggestive signs include systemic hypertension, progressive heart rate slowing and increasing muscle rigidity. These occur at intracranial pressures >30mmHg.

Management

- Correct/avoid potential aggravating factors, e.g. gut haemorrhage, over-sedation, hypoxia, hypoglycaemia, infection, electrolyte imbalance.

- Consider early intracranial pressure (ICP) monitoring. CT and clinical features correlate poorly with ICP though no controlled studies have yet been performed to show outcome benefit from ICP monitoring which carries its own complication rate (bleeding, infection).

- Maintain patient in slight head-up position (20–30°).

- Regular lactulose, e.g. 20–30ml qds PO, to achieve 2–3 bowel motions/day.

- Dietary restriction of protein is now not encouraged as this promotes endogenous protein utilisation.

- Hyperventilation to achieve a $PaCO_2$ of 3.5–4kPa is often attempted but is frequently unsuccessful in achieving improvement. It may also compromise cerebral blood flow.

- Mannitol (0.5–1mg/kg over 20–30min) if serum osmolality <320mOsmol/kg and either a raised ICP or clinical signs of cerebral oedema persist. If severe renal dysfunction is present, use renal replacement therapy in conjunction with mannitol.

- Sodium benzoate (2g tds PO) may be considered if the patient is severely hyperammonaemic.

- If no response to above, consider barbiturate administration, e.g. thiopental infusion at 1–5mg/kg/h, ideally with ICP monitoring.

- If still no response, consider urgent liver transplantation.

- Exercise caution with concomitant drug usage.

Identification of patients unlikely to survive without transplantation

- Prothrombin time >100s

  Or any three of the following:

- Age <10 or >40 years

- Aetiology is hepatitis C, halothane, or other drug reaction

- Duration of jaundice pre-encephalopathy >2 days

- Prothrombin time >50s

- Serum bilirubin >225μmol/l

  If paracetamol-induced:

- pH <7.3 or prothrombin time >100s and creatinine >200μmol/l plus Grade 3 or 4 encephalopathy.

As only 50–85% of patients identified as requiring transplantation will survive long enough to receive one, the Regional Liver Unit should be informed soon after diagnosis of all possible candidates.

See also:

Chronic liver failure

Patients admitted to intensive care with chronic liver failure may develop specific associated problems:

- Acute decompensation—this may be secondary to infection, sedation, hypovolaemia, hypotension, diuretics, gastrointestinal haemorrhage, excess dietary protein and electrolyte imbalance.

- Infection—the patient may transmit infection, e.g. hepatitis A, B or C and, by being immunosuppressed, is also more prone to acquiring infections such as TB and fungi.

- Drug metabolism—as many drugs are all or part-metabolised by the liver and/or excreted into the bile, the drug action may be prolonged or slowed depending on whether the metabolites are active or not. Inparticular,

sedatives may have a greatly prolonged duration of action.

- Portal hypertension—results in ascites, varices and splenomegaly. Ascites may produce diaphragmatic splinting and is at risk of becoming infected. Drainage may incur a considerable protein loss. Varices may bleed while splenomegaly may result in thrombocytopenia. Renal failure is also recognised due to high intra-abdominal pressure.

- Bleeding—an increased risk is present due to decreased production of clotting factors (II, VII, IX, X), varices and splenomegaly related thrombocytopenia.

- Alcohol—the most frequent cause of cirrhosis in the western world; acute withdrawal may lead to delirium tremens with severe agitation, hallucinations, seizures and cardiovascular disturbances.

- 2° hyperaldosteronism—results in oliguria, salt and water retention.

- Increased tendency to jaundice, especially during critical illness.

Management

1. Ascites

    - Take specimens for microbiological analysis (including TB), protein and cytology. If WBC > 250 per high power field, give Gram negative antibiotic cover.

    - If present in large quantity, (i) decrease sodium and water intake, (ii) commence spironolactone PO (or potassium canrenoate IV) ± furosemide. Paracentesis ± colloid replacement, or ascitic reinfusion (if uninfected/non-pancreatitic in origin) may be considered, particularly if diaphragmatic splinting occurs.

2. Coagulopathy:

    - Vitamin K 10mg/day slow IV bolus for 2–3 days.

    - Fresh frozen plasma, platelets as necessary.

3. Hypoglycaemia—should be prevented by adequate nutrition or a 10% or 20% glucose infusion.

4. Adequate nutrition and vitamin supplementation.

5. Acute decompensation—avoid any precipitating causes, e.g. infection, sedation, hypovolaemia, electrolyte imbalance.

6. Drug administration—review type and dose regularly.

P.365

See also:

Neurological Disorders

Acute weakness

Severe acute weakness may require urgent intubation and mechanical ventilation if the FVC <1l or gas exchange deteriorates acutely.

Investigation

- Metabolic myopathies—exclude and treat hypophosphataemia, hypokalaemia, hypocalcaemia and hypomagnesaemia.

- Prolonged effects of muscle relaxants—a prolonged effect of suxamethonium will usually be clinically obvious and should prompt assessment of pseudocholinesterase levels. Suxamethonium effects will also be prolonged in myasthenics. Prolonged effects of non-depolarising muscle relaxants are suggested by a response to an anticholinesterase (neostigmine 0.5 mg by slow IV bolus with an anticholinergic). This should not be attempted if paralysis is complete. Patients with myasthenia gravis will also respond.

- Guillain–Barré syndrome—a lumbar puncture should be performed to confirm raised CSF protein with normal cells. If these features are not found but suspicion is strong, nerve conduction studies may demonstrate segmental demyelination with slow conduction velocities.

- Myasthenia gravis—fatigueable weakness or ptosis suggests myasthenia gravis; response to IV edrophonium

(Tensilon test) and a strongly positive acetylcholine receptor antibody titre confirm this diagnosis. A myasthenic syndrome associated with malignancy (Eaton–Lambert syndrome) involves pelvic and thigh muscles predominantly, tending to spare the ocular muscles.

- Other diagnoses are made largely on the basis of clinical suspicion and specific specialised tests.

General management

- FVC should be monitored 2–4-hrly and intubation and mechanical ventilation should follow if FVC <1l. Other indices of respiratory function are less sensitive. In particular, arterial blood gases may be maintained up to the point of respiratory arrest.

- Weak respiratory muscles lead to progressive basal atelectasis and sputum retention. Chest infection is a significant risk; regular chest physiotherapy with intermittent positive pressure breathing are required for prevention where mechanical ventilation is not necessary.

- Patients who are immobile are at risk of venous stasis and deep venous thrombosis. Prophylaxis with subcutaneous heparin is reasonable. Immobile patients also require attention to posture to prevent pressure sores and contractures.

- Weak bulbar muscles may compromise swallowing with consequent malnutrition or pulmonary aspiration. Enteral nutritional support via a nasogastric tube is necessary.

- In cases with coexistent autonomic neuropathy enteral nutrition may be impossible, necessitating parenteral nutritional support. These patients may also suffer arrhythmias and hypotension requiring appropriate support.

Causes of severe weakness

Common in ICU
Metabolic myopathies

Prolonged effects of muscle relaxants

Critical illness neuropathy or myopathy

Guillain–Barré syndrome

Myasthenia gravis

Pontine CVA

Substance abuse (especially benzene ring compounds)

Uncommon in ICU
Chronic relapsing polyneuritis

Endocrine myopathies

Sarcoid neuropathy

Poliomyelitis

Diphtheria

Carcinomatous neuropathy

Porphyria

Botulism

Familial periodic paralysis

Multiple sclerosis

Lead poisoning

Organophosphorus poisoning

See also:
Ventilatory support—indications, p4; IPPV—assessment of weaning, p18; Enteral nutrition, p80; Parenteral nutrition, p82; Pulmonary function tests, p94; Electrolytes $(Na^+, K^+, Cl^-, HCO_3^-)$, p146; Calcium, magnesium and phosphate, p148; Muscle relaxants, p240; Respiratory failure, p282; Guillain–Barré syndrome, p384; Myasthenia gravis, p386; ICU neuromuscular disorders, p388

Agitation/confusion
In the ICU, agitation and/or confusion are predominantly related to sepsis, cerebral hypoperfusion drugs or drug withdrawal. 'ICU psychosis', with loss of day–night rhythm and inability to sleep, is a common occurrence in the patient recovering from severe illness.

Commoner ICU causes

- Infection—including generalised sepsis, chest, cannula sites, urinary tract. Cerebral infection such as meningitis, encephalitis and malaria are relatively rare but should always be considered.

- Drug-related—(i) adverse reaction (particularly affecting the elderly), e.g. sedatives, analgesics, diuretics; (ii) withdrawal, e.g. sedatives, analgesics, ethanol; (iii) abuse, e.g. opiates, amphetamines, alcohol, hallucinogens.

- Metabolic—e.g. hypo- or hyperglycaemia, hypo- or hypernatraemia, hypercalcaemia, uraemia, hepatic encephalopathy, hypo- or hyperthermia, dehydration.

- Respiratory—infection, hypoxaemia, hypercapnia.

- Neurological—infection (meningo-encephalitis, malaria), post-head injury, space-occupying lesion (including haematoma), post-ictal, post-cardiac arrest.

- Cardiac—low output state, hypotension, endocarditis.

- Pain—full bladder (blocked Foley catheter), abdominal pain.

- Psychosis—'ICU psychosis', other psychiatric states.

Principles of management

1. Examine for signs of (i) infection (e.g. pyrexia, purulent sputum, catheter sites, neutrophilia, falling platelet count, CXR, meningism), (ii) cardiovascular instability (hypotension, increasing metabolic acidosis, oliguria, arrhythmias), (iii) covert pain, particularly abdominal and lower limbs (e.g. compartment syndrome, DVT), (iv) focal neurological signs (e.g. meningism, unequal pupils, hemiparesis), (v) respiratory failure (arterial blood gases), (vi) metabolic derangement (biochemical screen). If any of the above are found, treat as appropriate. Psychosis should not be assumed until treatable causes are excluded.

2. Reassure and calm the patient. Maintain quiet atmosphere and reduce noise levels. Attempt to restore day–night rhythm, e.g. by changing ambient lighting and use of oral hypnotic agents.

3. Consider starting, changing or increasing dose of sedative or major tranquilliser to control the patient. If highly agitated and likely to endanger themselves, rapid short term control can be achieved by a slow IV bolus of sedative. Consider propofol, a benzodiazepine, haloperidol or chlorpromazine in the smallest possible dose to achieve the desired effect; observe for hypotension, respiratory depression, arrhythmias and extra-pyramidal effects. Opiates may be needed, especially if pain or withdrawal is a factor. An ethanol infusion can be considered for delirium tremens resulting from alcohol withdrawal.

4. Sedation can be maintained by continuous infusion or intermittent injection, either regularly or as required. The less agitated patient may respond to IM injections of a major tranquilliser, though these should be avoided with concurrent coagulopathy.

Drug dosages for severe agitation

•Chlorpromazine—12.5 mg by slow IV bolus. Repeat, doubling dose, every 10–15 until effect. May need up to 100 mg. For regular prescription, give qds.
•Haloperidol—2.5 mg by slow iIV bolus. Repeat, doubling dose, every 10–15 minutes until effect. For regular prescription, give qds.
•Midazolam/diazepam—2–5 mg by slow IV bolus.
•Propofol—30–100 mg by slow IV bolus.
•Morphine—2.5–5 mg by slow IV bolus.

NB beware excessive central and respiratory depression with the above agents

See also:

IPPV—failure to tolerate ventilation, p12; Toxicology, p162; Sedatives, p238; Acute liver failure, p360; Chronic liver failure, p364; Thyroid emergencies, p446; Poisoning—general principles, p452; Amphetamines including Ecstasy, p462; Cocaine, p464; Infection—diagnosis, p480; Systemic inflammation/multiorgan failure, p484; Head injury (1), p504; Head injury (2), p506; Pyrexia (1), p518; Pyrexia (2), p520; Pain, p532

Generalised seizures

Control of seizures is necessary to prevent ischaemic brain damage, to reduce cerebral oxygen requirements and to reduce intracranial pressure. Where possible correct the cause and give specific treatment. A CT scan may be necessary to identify structural causes. Common causes include:

- Hypoxaemia

- Hypoglycaemia
- Hypocalcaemia
- Space-occupying lesions
- Metabolic and toxic disorders
- Drug withdrawal, e.g. alcohol, benzodiazepines, anticonvulsants
- Infection, especially meningoencephalitis
- Trauma
- Idiopathic epilepsy

Most seizures are self-limiting, requiring no more than protection from injury (coma position, protect head and do not force anything into the mouth).

Specific treatment

- Hypoxaemia should be corrected with oxygen (FIO_2 0.6–1.0).
- Intubation and ventilation if the airway is unprotected or $SpO_2 < 90\%$.
- Blood glucose should be measured urgently and hypoglycaemia corrected with IV 50 ml 50% glucose.
- Anticonvulsant levels should be corrected in known epileptics.
- Cerebral oedema should be managed with sedation, induced hypothermia, controlled hyperventilation and osmotic diuretics.
- In patients with a known tumour, arteritis or parasitic infection, high dose dexamethasone may be given.
- Thiamine 100 mg IV should be given to alcoholics.
- Consider surgery for space-occupying lesions, e.g. blood clot, tumour.

Anticonvulsants

Anticonvulsants are necessary where there are repeated seizures, a single seizure lasts >30 min or there is cyanosis.

- A benzodiazepine (e.g. lorazepam, diazepam) is the usual first line treatment.
- Phenytoin—a loading dose should be given intravenously if the patient has not previously received phenytoin. Phenytoin may not provide immediate control of seizures within the first 24 h.

If seizures continue appropriate anticonvulsants include:

- Magnesium sulphate.
- Clonazepam, which is particularly useful for myoclonic seizures.
- Thiopental or propofol infusion in severe intractable epilepsy.

With all anticonvulsants care should be taken to avoid hypoventilation and respiratory failure. However, mechanical ventilation will certainly be required if thiopental is used, and probably to maintain oxygenation in cases of continued seizures.

Other supportive treatment

Muscle relaxants prevent muscular contraction during seizures but will not prevent continued seizures. They may be necessary to facilitate mechanical ventilation but continuous EEG monitoring should be used to judge seizure control. Correction of circulatory disturbance is required to maintain optimal cerebral blood flow.

Drug dosages

Lorazepam	4 mg IV.
Diazepam	Initially 2.5–5 mg IV or PR. Further increments as necessary to a maximum of 20 mg.
Midazolam	Initially 2.5–5 mg IV or PR. Further increments as necessary to a maximum of 20 mg.
Phenytoin	Loading dose 18 mg/kg IV at a rate <50 mg/min with continuous ECG monitoring. Maintenance at 300–400 mg/day IV, IM or PO adjusted according to levels.
Magnesium sulphate	Initially 20 mmol over 3–5 min followed by 5–10 mmol/h by infusion as necessary.
Clonazepam	1 mg/h IV.
Thiopental	1–3 mg/kg IV followed by lowest dose to maintain control.
Propofol	0.5–2 mg/kg IV followed by 1–3 mg/kg/h.

Key trial

Treiman VA for the Veterans Affairs Status Epilepticus Cooperative Study Group. A comparison of four treatments for generalized convulsive status epilepticus. N Engl J Med. 1998; 339:792–8

Meningitis

This is a life-threatening condition demanding prompt treatment. As the classical presentation of meningism may be absent, suspect in those presenting with obtundation, agitation, seizures or focal neurology. Signs may be subtle or present insidiously in neutropenics and the elderly. Meningococcaemia presents with a prominent rash in 30% of cases while *Listeria monocytogenes* may cause early seizures and focal neurological defects.

Diagnosis

- Bacterial meningitis is primarily diagnosed by CSF examination. This is unnecessary with a classical meningococcal rash where the organism can be often cultured from the skin lesions. Lumbar puncture (LP) samples should be sent for urgent microscopy and culture, PCR, antigen virology, protein and glucose estimation (with concurrent plasma sample). Normal or lymphocytic CSF may be found in early pyogenic meningitis, especially *L. monocytogenes*.

- Raised ICP is common; unless confidently excluded, delay lumbar puncture (LP) but *not* antibiotics until after CT scanning. A normal CT scan does not completely exclude raised ICP.

- Empiric antibiotic therapy with concurrent steroids should be commenced immediately after taking blood cultures. The choice should be based on the patient's age. CSF cultures are positive in 50% if antibiotics are given compared to 60–90% in untreated cases.

- CSF bacterial antigen testing is available for most infecting organisms; sensitivity varies from 50–100% while specificity is high.

Management

1. Antibiotic therapy, usually for ≥10 days, though recent studies suggest equal efficacy with shorter courses.

2. Dexamethasone 10 mg qds for 4 days should be commenced with or just before the first dose of antibiotic, particularly for pneumococcal meningitis.

3. General measures include attention to fluid and electrolyte replacement, adequate gas exchange, nutrition, and skin care.

4. Management of raised intracranial pressure if present.

5. Give oral ciprofloxacin (adults only) or rifampicin to family and close social contacts of meningococcal and haemophilus meningitis. The index case should also receive this treatment before discharge home.

Aseptic meningitis

No organisms are identified by routine CSF analysis despite a high neutrophil and/or lymphocyte count. Causes include viruses (e.g. mumps, measles), Lyme disease, fungi, leptospirosis, listeriosis, brucellosis, atypical TB, sarcoidosis, SLE.

Encephalitis

Presenting features include drowsiness, coma, agitation, pyrexia, seizures and focal signs; meningism need not necessarily be present.

Causes:

- Bacterial (as for meningitis)

- Viruses (in particular, herpes simplex and post-measles, chicken pox, mumps infection). Herpes simplex classically affects the temporal lobe and can be diagnosed by EEG. Give aciclovir 10 mg/kg tds IV for 10 days.

Rarer causes include leptospirosis and brucellosis; the CSF reveals no organisms but a high lymphocyte count is present. If indicated, send CSF for acid fast stain (TB) and India Ink stain (*Cryptococcus*).

Typical CSF values in meningitis

	Pyogenic	Viral	Tuberculosis
Classical appearance	turbid	clear	fibrin web
Predominant cell type	polymorphs	lymphocytes	lymphocytes
Cell count/mm^3	>1000	<500	50–1500
Protein (g/l)	>1	0.5–1	1–5
CSF:blood glucose	<60%	>60%	<60%

Organisms and empiric starting antibiotic therapy

Organism	Patients often affected	Antibiotic and dosage regimen (alternatives in brackets)
Neisseria meningitidis (Meningococcus)	young adults	ceftriaxone 2–4 g IV od (cefotaxime 50 mg/kg IV 8-hrly) (benzylpenicillin 1.2 g IV 2–4-hrly) (chloramphenicol 12.5 mg/kg IV 6-hrly)
Streptococcus pneumoniae (Pneumococcus)	older adults	ceftriaxone 2–4 g IV od (cefotaxime 50 mg/kg IV 8-hrly) (chloramphenicol 12.5 mg/kg IV 6-hrly)
Haemophilus influenzae	children	ceftriaxone 20–50 mg/kg IV od (cefotaxime 50 mg/kg IV 8-hrly) (chloramphenicol 12.5 mg/kg IV 6-hrly)
Listeria monocytogenes	elderly, immuno-compromised	ampicillin 1g IV 4–6-hrly plus gentamicin 120 mg IV stat, then 80 mg 8–12-hrly (adjust by plasma levels)
Mycobacterium tuberculosis		quadruple therapy (rifampicin/isoniazid/ ethambutol /pyrazinamide)
Cryptococcus neoformans	immuno-compromised	amphotericin B starting at 250 µg/kg IV od + flucytosine 50 mg/kg IV 6-hrly
Staph. aureus		flucloxacillin 2 g IV 6-hrly

Key papers

de Gans J, et al. Dexamethasone in adults with bacterial meningitis. N Engl J Med 2002; 347:1549–56.

van de Beek D, et al. Corticosteroids in acute bacterial meningitis. Cochrane Database Syst Rev 2003; (3):CD004305. Review.

See also:

Intracranial haemorrhage

Extradural haemorrhage

Usually presents acutely after head injury. Characterised by falling Glasgow Coma Score progressing to coma, focal signs (lateralising weakness or anaesthesia, pupillary signs), visual disturbances and seizures. Treatment by random burr holes has been supplanted by directed drainage following CT scan localisation.

A conservative approach may be adopted for small haematomata but increasing size (assessed by regular CT scanning or clinical deterioration) are indications for surgical drainage.

Subdural haemorrhage

Classically presents days to weeks following head trauma with a fluctuating level of consciousness (35%), agitation, confusion, seizures and signs of raised intracranial pressure, localising signs, or a slowly evolving stroke. Diagnosis is made by CT scan. Treatment is by surgical drainage.

Intracerebral haemorrhage

Causes include hypertension, neoplasm, vasculitis, coagulopathy and mycotic aneurysms associated with bacterial endocarditis.

Clinical features include sudden onset coma, drowsiness and/or neurological deficit. Headache usually occurs only with cortical and intraventricular haemorrhage. The rate of evolution depends on the size and size of the bleed. The area affected is the putamen (55%), thalamus (10%), cerebral cortex (15%), pons (10%) and cerebellum (10%).

Diagnosis

CT scan is the definitive test. A coagulation and vasculitis blood screen may be indicated. Angiography is indicated if surgical repair is contemplated though not for drainage of blood clot.

Treatment

- Bed rest

- Supportive (e.g. hydration, nutrition, analgesia, ventilatory support)

- Physiotherapy

- Blood pressure control (maintain systolic BP <220–230 mmHg)

- Correct any coagulopathy

- Control raised intracranial pressure

- Surgery—contact Regional Centre, e.g. for evacuation of haematoma, repair/clipping of aneurysm

- Steroid therapy is ineffective

See also:

Subarachnoid haemorrhage

Pathology

- In 15% no cause is found; of the remainder, 80% are due to a ruptured aneurysm, 5% to arteriovenous malformations and 15% follow trauma.

- The anterior part of the Circle of Willis is affected in 85–90% of caseswhile 10–15% affect the vertebrobasilar system.

- There is a 30% risk of rebleeding for which the mortality is 40%. Those surviving a month have a 90% chance of surviving a year.
- Cerebral vasospasm occurs in 40–70% of patients at 4–12 days after the bleed. This is the most important cause of morbidity and mortality.
- Hydrocephalus, seizures, hyponatraemia and inappropriate ADH secretion are recognised complications.

Clinical features

- SAH may be preceded by a prodrome of headache, dizziness and vague neurological symptoms.
- Often there is rapid onset (minutes to hours) presentation including collapse, severe headache ± meningism.
- Cranial nerve palsies, drowsiness and hemiplegia may also occur.

Diagnosis

Diagnosis is usually made by CT scan; if there is no evidence of raised intracranial pressure, a lumbar puncture may be performed revealing blood-stained CSF with xanthochromia.

Management

- Bed rest.
- Maintain adequate hydration, nutrition, analgesia, sedation.
- Cerebral vasospasm is prevented by nimodipine infusion and maintenance of a full intravascular volume.
- Systemic hypertension should only be treated if severe (e.g. systolic pressure >220–230 mmHg) and prolonged.
- Surgery—the timing is controversial with either early or delayed (7–10 days) intervention being advocated. The Regional Neurosurgical Centre should be consulted for local policy.
- Antifibrinolytic therapy (e.g. tranexamic acid) reduces the incidence of rebleeding but has no beneficial effect on outcome.

Key trial

Allen GS, et al. Cerebral arterial spasm—a controlled trial of nimodipine in patients with subarachnoid hemorrhage. N Engl J Med 1983; 308:619–24

See also:

Ventilatory support—indications, p4; Blood pressure monitoring, p110; Intracranial pressure monitoring, p134; Coagulation monitoring, p156; Neuroprotective agents, p244; Basic resuscitation, p270; Hypertension, p314; Generalised seizures, p372; Intracranial haemorrhage, p376; Raised intracranial pressure, p382; Bleeding disorders, p396; Brain stem death, p548; Withdrawal and witholding treatment, p550; Care of the potential organ donor, p552

Stroke

Pathology

- Haemorrhage, embolus or thrombosis.
- 'Secondary' stroke may occur with meningitis, bacterial endocarditis, subarachnoid haemorrhage and vasculitis.
- Dissection and cerebral venous thrombosis need to be considered, as anticoagulation is indicated for both (unless a large infarct is established, as there is an increased risk of bleeding). Dissection should be suspected in younger patients, often presenting with severe headache or neck pain ± Horner's syndrome ± seizures after trauma or neck manipulation. Cerebral venous thrombosis may mimic stroke, tumour, subarachnoid haemorrhage or meningo-encephalitis and may present with headache, seizures, focal signs or obtundation.

Urgent CT scan

Indicated when the diagnosis is in doubt, for continuing deterioration, suspicion of subarachnoid haemorrhage, hydrocephalus or trauma, or for patients who are anticoagulated or who have a bleeding tendency.

Aims of treatment

- To protect the penumbra with close attention to oxygenation, hydration, glycaemic control, and avoidance of pyrexia.
- Blood pressure control is needed for severe hypertension (e.g. >200/120 mmHg) and hypotension.
- Drug therapy including thrombolysis and aspirin. The evidence for anticoagulation remains contentious as there is an increased risk of bleeding and no consistent subgroup benefit has been shown. Early anticoagulation is

probably beneficial for intracranial stenosis, a stroke-in-evolution, complete vessel occlusion with minimal deficit and in low risk patients with a high probability of recurrence (secondary prevention).

- For thrombolysis the extent of reperfusion depends on the aetiology with basilar > middle cerebral artery > internal carotid, and embolic > thrombotic. Pooled studies with rt-PA (0.9 mg/kg) given within 3 h of stroke onset (and tight blood pressure control) showed a favourable outcome. However, there was a 6-fold increase in haemorrhage (to 5.9%), of whom 60% died. This was more common in the elderly, and with more severe stroke.

- Neurosurgical intervention may be considered for cerebellar haematoma, cerebellar infarction and the malignant middle cerebral artery syndrome (for massive infarction on the non-dominant side).

Key paper

Hacke W, et al. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. Lancet 2004; 363:768–74

See also:

Raised intracranial pressure

Clinical features

- Headache, vomiting, dizziness, visual disturbance
- Seizures, focal neurology, papilloedema
- Increasing blood pressure, bradycardia (late responses)
- Agitation, increasing drowsiness, coma
- Slow deep breaths, Cheyne–Stokes breathing, apnoea
- Ipsilateral progressing to bilateral pupillary dilatation
- Decorticate progressing to decerebrate posturing

Diagnosis

- CT scan or MRI
- Intracranial pressure (ICP) measurement >20 mmHg

Lumbar puncture should be avoided because of the risk of coning.

Neither CT scan nor absence of papilloedema will exclude a raised ICP.

Causes

- Space-occupying lesion (e.g. neoplasm, blood clot, abscess)
- Increased capillary permeability (e.g. trauma, infection, encephalopathy)
- Cell death (e.g. post-arrest hypoxia)
- Obstruction (e.g. hydrocephalus)

Management

1. Bed rest, 20–308 head-up tilt, sedation, quiet environment, minimal suction and noise. Sedation is often necessary to overcome a hyperadrenergic state but sedative-induced hypotension should be avoided. The tape tethering the endotracheal tube in place should not occlude jugular venous drainage.

2. Ventilate if GCS ≤8, airway unprotected or excessively agitated.

3. Maintain $PaCO_2$ at 4–4.5 kPa and avoid rapid rises. CSF bicarbonate levels re-equilibrate within 4–6 h, negating any benefit from hyperventilation.

4. If possible, monitor ICP. Aim to maintain ICP <20 mmHg and cerebral perfusion pressure (CPP=MAP-ICP) ≥70 mmHg. Vasopressors may be needed. Do not treat systemic hypertension unless very high (e.g. systolic >220–230 mmHg).

5. Jugular bulb venous saturation (SjO_2) and lactate may be useful monitoring techniques though do not detect regional ischaemia.

6. Give mannitol 0.5 mg/kg over 15 min. Repeat 4-hrly depending on CPP measurements and/or clinical signs of

deterioration. Stop when plasma osmolality reaches 310–320 mOsmol/kg.

7. Avoid severe alkalosis as cerebral vascular resistance rises and cerebral ischaemia increases.

8. Consider specific treatment, e.g. for meningo-encephalitis, malaria, hepatic encephalopathy, surgery. Some neurosurgeons decompress the cranium for generalised oedema by removing a skull flap. Seek local advice. Dexamethasone 4–16 mg qds IV is beneficial for oedema surrounding a tumour or abscess and for herpes simplex encephalitis.

Acute deterioration/risk of imminent coning

1. Mechanically ventilate to PaCO2 3.0–3.5 kPa for 10–20 min.

2. Give mannitol 0.5 g/kg IV over 15 min. Repeat 4-hrly as necessary while plasma osmolality <310–320 mOsmol/kg. Consider furosemide.

3. If no response in ICP, CPP and/or clinical features, give thiopental (successful in 50% of resistant cases).

4. Consider repeat CT scan and refer for urgent surgery if a surgically amenable space-occupying lesion is diagnosed.

See also:

Ventilatory support—indications, p4; Blood pressure monitoring, p110; Intracranial pressure monitoring, p134; Diuretics, p212; Neuroprotective agents, p244; Basic resuscitation, p270; Hypertension, p314; Generalised seizures, p372; Intracranial haemorrhage, p376; Subarachnoid haemorrhage, p378; Stroke, p380; Head injury (1), p504; Head injury (2), p506; Brain stem death, p548; Withdrawal and witholding treatment, p550; Care of the potential organ donor, p552

Guillain–Barré syndrome

This is an immunologically-mediated, acute demyelinating polyradiculopathy. Viral infections and immunisations are common antecedents. The syndrome includes a progressive, areflexic motor weakness (often symmetrical, ascending and involving cranial nerves including facial, bulbar and extraocular) with progression over days to weeks. There are often minor sensory disturbances (e.g. paraesthesiae). Autonomic dysfunction is not unusual. There is no increase in cell count on CSF examination but protein levels usually rise progressively (>0.4 g/l). Nerve conduction studies show slow conduction velocities with prolonged F waves. Other features include muscle tenderness and back pain. The major contributors to morbidity and mortality are respiratory muscle weakness and autonomic dysfunction (hypotension, hypertension, arrhythmias, ileus and urinary retention).

Differential diagnosis

Other causes of acute weakness must be excluded before a diagnosis of Guillain–Barré syndrome can be made.

Specific treatment

- Intravenous gammaglobulin (0.4 g/kg/day for 5 days) or plasma exchange (five 50 ml/kg exchanges over 8–13 days) is effective if started within 14 days of onset of symptoms.

- Steroids have not been shown to be beneficial.

Supportive treatment

Respiratory care

Regular chest physiotherapy and spirometry are required. Mechanical ventilation is needed if FVC <1l or PaCO$_2$ is raised. An early tracheostomy is useful since mechanical ventilation is likely to continue for several weeks. Patients with bulbar involvement or inadequate cough should undergo tracheotomy, even if spontaneous breathing continues.

Cardiovascular care

Continuous cardiovascular monitoring is required due to the effects of autonomic involvement. Arrhythmias are particularly likely with anaesthesia (especially with suxamethonium). Hypertensive and hypotensive responses are generally exaggerated with vasoactive drugs.

Nutritional support

Parenteral nutrition will be required in cases where there is ileus. Enteral nutrition is preferred, if possible, even though energy and fluid requirements are reduced in Guillain–Barré syndrome.

Analgesia

Analgesia is required for muscle, abdominal and back pain. Although NSAIDs may be useful, opiates are often required.

Other support

Particular attention is required to pressure areas and deep vein thrombosis prophylaxis.

Key trials

Plasma Exchange/Sandoglobulin Guillain-Barre Syndrome Trial Group. Randomised trial of plasma exchange, intravenous immunoglobulin, and combined treatments in Guillain-Barré syndrome. Lancet 1997; 349:225–30

van Koningsveld R, for the Dutch GBS study group. Effect of methylprednisolone when added to standard treatment with intravenous immunoglobulin for Guillain–Barre syndrome: randomised trial. Lancet 2004; 363:192–6

See also:

Ventilatory support—indications, p4; Blood pressure monitoring, p110; Neuroprotective agents, p244; Basic resuscitation, p270; Hypertension, p314; Generalised seizures, p372; Intracranial haemorrhage, p376; Subarachnoid haemorrhage, p378; Raised intracranial pressure, p382

Myasthenia gravis

Myasthenia gravis is associated with painless weakness which is worse after exertion with deterioration during stress, infection or trauma.

Tendon reflexes are normal. It is an autoimmune disease associated with acetylcholine receptor and, rarely, anti-striated muscle antibodies.

There is also an association with other autoimmune diseases (e.g. thyroid disease, SLE, rheumatoid arthritis).

Younger (<45 years), predominantly female patients may have a thymoma which, if resected, may provide remission.

Severe weakness may be the result of a myasthenic or cholinergic (e.g. sweating, salivation, lacrimation, colic, fasciculation, confusion, ataxia, small pupils, bradycardia, hypertension, seizures) crisis.

Diagnosis of myasthenia

Edrophonium is a short acting anticholinesterase used in the diagnosis of myasthenia in patients with no previous history of myasthenia gravis. In myasthenic patients with an acute deterioration the test may distinguish a myasthenic from a cholinergic crisis. In cholinergic crisis there is a possibility of further deterioration and atropine and facilities for urgent intubation and ventilation should be available. An initial dose of 2 mg IV is given. If there are no cholinergic side-effects a further 8 mg may be given. A positive test is judged by improvement of weakness within 3 min of injection. The test may be combined with objective assessment of respiratory function by measuring the FVC response or by assessing the response to repetitive stimulation with an EMG.

Maintenance treatment

Anticholinesterase drugs provide the mainstay of symptomatic treatment but steroids, immunosuppressives and plasma exchange may provide pharmacological remission.

Myasthenic crisis

New myasthenics may present in crisis and treatment should be started with steroids, azathioprine and pyridostigmine. Plasma exchange may be useful to reduce the antibody load. In known myasthenics an increased dose of pyridostigmine and steroids will be required. If the condition deteriorates drug therapy should be stopped; plasma exchange may be life saving. Anticholinesterases may produce improvement in some muscle groups and cholinergic deterioration in others due to differential sensitivity. As with any case of acute weakness mechanical ventilatory support is required if FVC <1l or the $PaCO_2$ is raised.

Cholinergic crisis

Cholinergic symptoms are usually at their most severe 2 h after the last dose of anticholinesterase. It is common to give atropine prophylactically in the treatment of myasthenia which may mask some of the cholinergic symptoms. If a deterioration of myasthenia fails to respond to edrophonium all drugs should be stopped and atropine given (1 mg IV every 30 min to a maximum of 8 mg). The edrophonium test should be repeated every 2 h and anticholinesterases reintroduced when the test is positive. Mechanical ventilation is required if FVC <1l or the $PaCO_2$ is raised.

Drug dosages

Prednisolone	80 mg/day orally
Azathioprine	2.5 mg/kg/day orally
Pyridostigmine	60–180 mg 6-hrly orally
Atropine	0.6 mg 6-hrly orally

Drugs causing a deterioration in myasthenia

Aminoglycosides

Streptomycin

Tetracyclines

Local anaesthetics

Muscle relaxants

Opiates

See also:

Ventilatory support—indications, p4; Endotracheal intubation, p36; Special support surfaces, p86; Plasma exchange, p68; Pulmonary function tests, p94; Steroids, p262; Respiratory failure, p282; Hypotension, p312; Tachyarrhythmias, p316; Bradyarrhythmias, p318; Acute weakness, p368

ICU neuromuscular disorders

Neuromuscular disorders in the critically ill have long been recognised, particularly in those being mechanically ventilated. First suspicions are often raised when patients fail to wean from mechanical ventilation or limb weakness is noted on stopping sedation. Disuse atrophy, catabolic states and drug therapy (e.g. high dose steroids, muscle relaxants) are probably responsible for some cases but do not explain all. A neuromyopathic component of multi-organ dysfunction syndrome may be implicated.

Critical illness neuropathy

Neurophysiological studies have demonstrated an acute idiopathic axonal degeneration in patients with a flaccid weakness following a prolonged period of intensive care. Nerve conduction velocities are normal indicating no demyelination. CSF is normal unlike Guillain–Barré syndrome. The neuropathy is self-limiting but prolongs the recovery phase of critical illness. Recovery may take weeks to years. Pyridoxine (100–150 mg daily PO) has been used in the treatment.

Critical illness myopathy

Drug induced myopathy is not uncommon in critically ill patients. Steroid induced myopathy is less common as the indications for high dose steroids have been reduced. Muscle relaxants may have a prolonged effect and may be potentiated by β_2 agonists. Muscle histological studies have demonstrated abnormalities (fibre atrophy, mitochondrial defects, myopathy and necrosis) which could not be associated with steroid or muscle relaxant therapy. Myopathy may cause renal damage via myoglobinuria. Critical illness myopathy is associated with various forms of muscle degeneration but is usually self-limiting. Recovery may take weeks to years.

See also:

Ventilatory support—indications, p4; IPPV—assessment of weaning, p18; Special support surfaces, p86; Pulmonary function tests, p94; Respiratory failure, p282; Acute weakness, p368; Guillain–Barré syndrome, p384

Tetanus

The clinical syndrome is caused by the exotoxin tetanospasmin from the anaerobe *Clostridium tetani* in contaminated or devitalised wounds. Tetanospasmin ascends intra-axonally in motor and autonomic nerves, blocking release of inhibitory neurotransmitters. The disease may be modified by previous immunisation, thus milder or localised symptoms occur with heavier toxin loads.

Clinical features

- Gradual onset of stiffness, dysphagia, muscle pain, hypertonia, rigidity and muscle spasm.
- Laryngospasm often follows dysphagia.
- Muscle spasm is often provoked by minor disturbance, e.g. laryngospasm may be provoked by swallowing.

- Onset of symptoms within 5 days of injury implies a heavy toxin load and severe disease.
- The disease is self-limiting so treatment is supportive but may need to continue for several weeks.

Management of the wound

If a contaminated wound is present, it should be debrided surgically to remove the source of the toxin. Benzylpenicillin 1.2 g 6-hrly and metronidazole 500 mg 8-hrly IV are appropriate antibiotics.

Passive immunisation

Human tetanus immunoglobulin 1000–1500 units IM may shorten the course of the disease by removing circulating toxin. Rapid fixation of the toxin to tissues limits the usefulness of this approach.

Mild tetanus

Patients with mild symptoms, no respiratory distress and a delayed onset of symptoms should be nursed in a quite environment with mild sedation to prevent tetanic spasms.

Severe tetanus

- Intubate and ventilate since asphyxia may occur due to prolonged respiratory muscle spasm.
- Sedation may be achieved with diazepam (20 mg 4–6-hrly NG and 5 mg IV as necessary).
- Muscle rigidity is best treated with magnesium sulphate 20 mmol/h IV ± chlorpromazine 25–75 mg 4-hrly IV or NG, with muscle relaxants if necessary.
- Autonomic hyper-reactivity is a feature (arrhythmias, hypotension, hypertension and myocardial ischaemia). It is minimised by sedation, anaesthesia and treated by atropine 1–20 mg/h IV, propranolol 10 mg 8-hrly IV or NG, and magnesium sulphate 20 mmol/h IV.

Tetanus toxoid prophylaxis

The disease confers no immunity so patients must be immunised prior to hospital discharge.

- Last dose of tetanus toxoid >5 years no further dose
- Last dose of tetanus toxoid <10 years 1 dose
- No previous immunisation 3 doses

See also:

Ventilatory support—indications, p4; Sedatives, p238; Muscle relaxants, p240; Antimicrobials, p260; Respiratory failure, p282; Hypotension, p312; Hypertension, p314; Tachyarrhythmias, p316; Bradyarrhythmias, p318

Botulism

An uncommon, lethal disease caused by the exotoxins of the anaerobe *Clostridium botulinum.* Botulism is most commonly a food-borne disease, especially associated with canned foods. It may be contracted by wound contamination with aquatic soils. The toxin is carried in the blood to cholinergic neuromuscular junctions where it binds irreversibly. Symptoms begin between 6 h and 8 days after contamination and are more severe with earlier onset. Botulism is diagnosed by isolating *Clostridium botulinum* from the stool or by mouse bioassay (survival of immunised mice and death of non-immunised mice when infected serum is injected).

Clinical features

- Symptoms include gastrointestinal disturbance, sore throat, fatigue, dizziness, paraesthesiae, cranial involvement and a progressive, descending flaccid weakness.
- Parasympathetic symptoms are common.
- The disease is usually self-limiting within several weeks.

Respiratory care

Regular spirometry and mechanical ventilation if FVC <1l. Patients with bulbar palsy need intubation for airway protection.

Toxin removal

If there is no ileus the use of non-magnesium containing cathartics may remove the toxin load. Magnesium may enhance the effect of the toxin.

Antitoxin

May shorten the course of the disease if given early and the toxin type is known (seven have been identified). There is a high risk of anaphylactoid reactions.

Wound botulism
Surgical debridement and penicillin are the mainstay of treatment for contaminated wounds.

See also:

Ovid: Oxford Handbook of Critical Care

Haematological Disorders

Bleeding disorders
A common problem in the critically ill, this may be due to (i) large vessel bleeding—usually 'surgical' or following a procedure (e.g. chest drain, tracheostomy, accidental arterial puncture, removal of intravenous or intra-arterial catheter); peptic ulcer bleeding is now relatively uncommon due to improved attention to perfusion and nutrition; (ii) around vascular catheter sites or from intubated/instrumented lumens and orifices—usually related to severe multisystem illness or excess anticoagulant therapy, including thrombolytics; (iii) small vessel bleeding, e.g. skin petechiae, gastric erosions—usually related to anticoagulation or severe generalised illness including disseminated intravascular coagulation.

A falling platelet count is often an early sign of sepsis and critical illness. Recovery of the count usually coincides with overall patient recovery.

Common ICU causes

- Decreased platelet production, e.g. sepsis- or drug-induced

- Decreased production of coagulation factors, e.g. liver failure

- Increased consumption, e.g. DIC, major trauma, bleeding, heparin-induced thrombocytopenia, antiplatelet antibodies, extracorporeal circuits

- Impaired or deranged platelet function

- Drugs, e.g. heparin, aspirin

- Decreased protease inhibitors, e.g. antithrombin III, Protein S and Protein C deficiency (following sepsis)

Principles of management

1. An International Normalised Ratio (INR) between 1.5–2.5 and/or platelet count of $(20–40) \times 10^9$/l do not usually require correction if the patient is not bleeding or at high risk e.g. active peptic ulcer, recent cerebral haemorrhage, undergoing an invasive procedure. 5–10 units of platelets will raise the count by only $10–20 \times 10^9$/l. The effect is often transient (<24 h) and the increment reduces with repetitive dosing. Treatment of symptomatic thrombocytopenia aims to increase the count $>50 \times 10^9$/l. A target INR <1.5 is acceptable. Vitamin K is given for liver failure and considered for warfarin overdosage. 1 mg Vitamin K will reverse warfarin effects within 12 h while 10 mg will saturate liver stores, preventing warfarin activity for some weeks. Fresh frozen plasma (FFP) is given for short term control.

2. If bleeding and INR = 1.5–2, give 2–3 units FFP. If INR >2, give 4–6 units FFP. If not bleeding (or high risk), generally only correct if INR >2.5–3. Repeat clotting screen 30–60 min after FFP infused. Give more FFP if bleeding continues and/or INR >3.

3. For bleeding related to thrombolysis, (i) stop the drug infusion, (ii) give either aprotinin 500,000 units over 10 min, then 200,000 units over 4 h or tranexamic acid 10 mg/kg repeated 6–8-hrly (iii) give 4 units FFP.

4. Cryoprecipitate is rarely needed. Consider when the thrombin time is elevated, e.g. with DIC. Similarly, factor VIII is generally used for haemophiliacs only.

5. If aspirin has been taken within the past 1–2 weeks, platelet function may be deranged. Give fresh platelets, even though count may be adequate.

6. Factor VIIa may be useful for severe, intractable bleeding but more studies are needed to confirm its efficacy.

Management of major bleeding

1. If external, direct occlusion/deep suture.

2. Urgent expert opinion—e.g. for surgery, endoscopy + injection, etc.

3. Correct coagulopathy.

Management of vascular catheter or percutaneous drain site bleeding

1. Direct pressure/occlusive dressing.

2. Correct coagulopathy; consider use of aprotinin or tranexamic acid.

3. Surgical intervention is rarely necessary although perforation/laceration of local artery/vein should be considered if bleeding fails to stop or becomes significant.

See also:

Coagulation monitoring, p156; Blood transfusion, p182; Blood products, p252; Coagulants and antifibrinolytics, p254; Aprotinin, p256; Haemoptysis, p304; Upper gastrointestinal haemorrhage, p344; Lower intestinal bleeding and colitis, p348; Acute liver failure, p360; Chronic liver failure, p364; Platelet disorders, p406; Systemic inflammation/multiorgan failure, p484; Post-operative intensive care, p534

Clotting disorders

Uncommon as a secondary event in critically ill patients as they tend to be auto-anticoagulated. The risk of major venous thrombosis increases with long term immobility and paralysis, and in specific pro-thrombotic conditions such as pregnancy, thrombotic thrombocytopenic purpura, SLE (lupus anticoagulant), sickle cell crisis, hyperosmolar diabetic coma.

Disseminated intravascular coagulation is associated with microvascular clotting, a consumption coagulopathy and increased fibrinolysis.

Clotting of extracorporeal circuits, e.g. for renal replacement therapy, may be due to (i) mechanical obstruction to flow, e.g. kinked catheter, (ii) inadequate anticoagulation or (iii) in severe illness, a decrease in endogenous anticoagulants (e.g. antithrombin III); this may result in circuit blockage despite a coexisting thrombocytopenia and/or coagulopathy.

Axillary vein or subclavian vein thrombosis may result from indwelling intravenous catheters.

Management

If the patient is not auto-anticoagulated, prophylactic low molecular weight heparin (5000 IU od SC) should be given for long term immobility/paralysis and to high risk patients (e.g. previous DVT, femoral fractures).

For pulmonary embolism or deep vein thrombosis give 200 IU/kg SC daily (or 100 IU/kg bd if at risk of bleeding).

Partial thromboplastin times (PTT) should be checked regularly if giving unfractionated heparin and maintained at approximately 2–3 × normal. Monitoring is not necessary for LMW heparin though anti-Factor Xa levels can be used.

Intra-arterial clot can be treated with local infusion of thrombolytics, usually followed by heparinisation. Seek vascular surgical advice.

Axillary vein or subclavian vein thrombosis should be managed by elevation of the affected arm, e.g. in a Bradford sling, and heparinisation.

Specific conditions may require specific therapies, e.g. plasma exchange for SLE and TTP, whole blood exchange for sickle cell crisis.

Warfarinisation should generally be avoided until shortly before ICU discharge because of the risk of continued bleeding following routine invasive procedures such as central venous catheterisation.

See also:

Coagulation monitoring, p156; Anticoagulants, p248; Thrombolytics, p250; Blood products, p252; Pulmonary embolus, p308

Anaemia

Defined as a low haemoglobin due to a decreased red cell mass, it may also be 'physiological' due to dilution from an increased plasma volume, e.g. pregnancy, vasodilated states.

Major causes in the ICU patient

- Blood loss, e.g. haemorrhage, regular blood sampling
- Severe illness—analogous to the 'anaemia of chronic disease', there is decreased marrow production and,

possibly, a decreased lifespan

Rarer causes include:

- Microcytic anaemia—predominantly iron deficiency
- Normocytic
- Chronic disease
- Bone marrow failure (idiopathic, drugs, neoplasm, radiation)
- Haemolysis
- Renal failure
- Macrocytic—vitamin B_{12} and folate deficiency, alcoholism, cirrhosis, sideroblastic anaemia, hypothyroidism
- Congenital diseases—sickle cell, thalassaemia

Management

1. Treatment of the cause where possible.
2. Blood transfusion:
    - The ideal haemoglobin level for optimal oxygen carriage and viscosity remains contentious. A recent multicentre trial showed improved outcomes if a trigger of 7 g/dl was used. A higher transfusion threshold, e.g. 9–10 g/dl, may be needed in those with cardiorespiratory disease.
    - Transfusion is usually given as packed cells with or without a small dose of furosemide to maintain fluid balance. This may need to be given rapidly during active blood loss, or slowly for correction of a gradually falling haemoglobin level.
    - Rarely, patients admitted with a chronically low haemoglobin, e.g. <4–5 g/dl, which often follows long term malnutrition or vitamin deficiency, will need a much slower elevation in haemoglobin level to avoid precipitating acute heart failure. An initial target of 7–8 g/dl is often acceptable. Obviously, this may need to be altered in the light of any concurrent acute illness where elevation of oxygen delivery is deemed necessary.
    - Erythropoeitin reduces the need for blood transfusion in long-term ICU patients and may be useful in those with multiple antibodies or declining transfusion for religious reasons.

Key trial

Hebert PC, et al for the Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. N Engl J Med 1999; 340:409–17

Sickle cell disease

A chronic, hereditary disease almost entirely confined to the black population where the gene for Hb S is inherited from each parent. The red blood cells lack Hb A; when deprived of oxygen these cells assume sickle and other bizarre shapes resulting in erythrostasis, occlusion of blood vessels, thrombosis and tissue infarction. After stasis, cells released back into the circulation are more fragile and prone to haemolysis. Occasionally, there may be bone marrow failure.

Chronic features

Patients with sickle cell disease are chronically anaemic (7–8 g/dl) with a hyperdynamic circulation. Splenomegaly is common in youth but, with progressive episodes of infarction, splenic atrophy occurs leading to an increased risk of infection, particularly pneumococcal.

Chronic features include skin ulcers, renal failure, avascular bone necrosis (± supervening osteomyelitis, especially *Salmonella*), hepatomegaly, jaundice and cardiomyopathy. Sudden cardiac death is not uncommon, usually before the age of 30.

Sickle cell crises

Crises are precipitated by various triggers, e.g. hypoxaemia (air travel, anaesthesia, etc.), infection, cold, dehydration and emotional stress.

Thrombotic crisis

Occurs most frequently in bones or joints but also affects chest and abdomen giving rise to severe pain. Neurological symptoms (e.g. seizures, focal signs), haematuria or priapism may be present. Pulmonary crises are the commonest

reason for ICU admission; secondary chest infection or ARDS may supervene, worsening hypoxaemia and further exacerbating the crisis.

Aplastic crisis
Related to parvovirus infection, it is suggested by worsening anaemia and a reduction in the normally elevated reticulocyte count (10–20%).

Haemolytic crisis
Intravascular haemolysis with haemoglobinuria, jaundice and renal failure sometimes occurs.

Sequestration crisis
Rapid hepatic and splenic enlargement due to red cell trapping with severe anaemia. This condition is particularly serious.

Management
Prophylaxis against crises includes avoidance of hypoxaemia and other known precipitating factors, prophylactic penicillin and pneumococcal vaccine, and exchange transfusions.

1. Painful crises usually require prompt opiate infusions. Although psychological dependence is high, analgesia should not be withheld.

2. Give oxygen to maintain SaO_2 at 100%.

3. Rehydrate with intravenous fluids and keep warm.

4. If infection is suspected, antibiotics should be given as indicated.

5. Transfuse blood if haemoglobin level drops or central nervous system or lung complications present.

6. Lower proportion of sickle cells to <30% by exchange transfusion.

7. Mechanical ventilation may be necessary for chest crises.

See also:
Oxygen therapy, p2; Pulse oximetry, p90; Full blood count, p154; Bacteriology, p158; Acute chest infection (1), p288; Acute chest infection (2), p290; Acute renal failure—diagnosis, p332; Acute renal failure—management, p334; Jaundice, p358; Anaemia, p400; Haemolysis, p404

Haemolysis
Shortening of erythrocyte lifespan below the expected 120 days. Marked intravascular haemolysis may lead to jaundice and haemoglobinuria.

Causes

- Blood transfusion reactions

- Haemolytic uraemic syndrome (microangiopathic haemolytic anaemia)

- Trauma (cardiac valve prosthesis)

- Malaria

- Sickle cell haemolytic crisis

- Drugs—e.g. high-dose penicillin, methyl dopa

- Autoimmune (cold- or warm antibody-mediated)—may be idiopathic or secondary, e.g. lymphoma, SLE, mycoplasma

- Glucose-6-phosphate dehydrogenase deficiency—oxidative crises occur following ingestion of fava beans, primaquine, sulphonamides leading to rapid onset anaemia and jaundice

Diagnosis

- Unconjugated hyperbilirubinaemia, increased urinary urobilinogen (increased RBC breakdown)

- Reticulocytosis (increased RBC production)

- Splenic hypertrophy (extravascular haemolysis)

- Methaemoglobinaemia, haemoglobinuria, free plasma haemoglobin (intravascular haemolysis), reduced serum haptoglobins

- RBC fragmentation (microangiopathic haemolytic anaemia)

- Coombs' test (immune-mediated haemolysis)

- Other (including haemoglobin electrophoresis, bone marrow biopsy)

Management

1. Identification and specific treatment of the cause where possible.

2. Blood transfusion to maintain haemoglobin >7g/dl

3. Massive intravascular haemolysis may lead to acute renal failure. Maintain a good diuresis and haemo(dia)filter if necessary.

See also:

Full blood count, p154; Blood transfusion, p182; Acute renal failure—diagnosis, p332; Acute renal failure—management, p334; Jaundice, p358; Anaemia, p400; Sickle cell disease, p402; Platelet disorders, p406; Malaria, p490; Vasculitides, p494; HELLP syndrome, p540

Platelet disorders

Thrombocytopenia

Rarely symptomatic until the platelet count <50 × 10^9/l; spontaneous bleeding is more likely <20 × 10^9/l. Although bleeding is often minor, e.g. skin petechiae, oozing at intravascular catheter sites, it may be massive or life-threatening, e.g. haemoptysis, intracranial haemorrhage.

Causes

- Sepsis—in the ICU this is the commonest cause of a low platelet count; often provides a good barometer of recovery or deterioration
- Disseminated intravascular coagulation
- Drugs
- Related to antiplatelet antibody production, e.g. heparin (heparin-induced thrombocytopenia syndrome, 'HITS'), sulphonamides, quinine
- Resulting in bone marrow suppression, e.g. chemotherapy agents
- Others, e.g. aspirin, chlorpromazine, prochlorperazine, digoxin
- Following massive bleeding and multiple blood transfusions
- Bone marrow failure, e.g. tumour infiltration, drugs
- Splenomegaly
- Thrombotic thrombocytopenic purpura (TTP), haemolytic uraemic syndrome (HUS)
- Idiopathic thrombocytopenic purpura (ITP)
- Specific infections, e.g. measles, infectious mononucleosis, typhus
- Collagen vascular diseases, e.g. SLE

Management

1. Directed at the cause, e.g. antibiotics for sepsis, stopping offending drugs, plasma exchange for TTP, splenectomy and steroids for ITP.

2. Platelet support
   - Given routinely (e.g. 6–10 units/day) when counts <10–20 × 10^9/l
   - 6–10 units given if <50 × 10^9/l and either symptomatic or due to undergo surgery or another invasive procedure

3. Unless actively bleeding, avoid platelet transfusions in TTP or HUS.

Deranged platelet function

Function may be deranged, albeit with normal counts, e.g. following aspirin within past 1–2 weeks, epoprostenol, uraemia. Fresh platelets may be required if the patient is symptomatic. In uraemia, one dose of vasopressin (20µg IV over 30 min) may be useful before surgery.

Thrombocythaemia

Rare in ICU patients; platelet counts often exceed 800 × 10^9/l.

Causes

Prolonged low-level bleeding, post-splenectomy, myeloproliferative disorders. Essential (idiopathic) thrombocythaemia is unusual.

Management

As the major risk is thrombosis, management is based upon mobilising the patient and administration of either prophylactic aspirin (150 mg bd PO) or LMW heparin (5000 IU od SC). Dipyridamole (300–600 mg tds PO) is occasionally used.

See also:

Plasma exchange, p68; Full blood count, p154; Blood transfusion, p182; Anticoagulants, p248; Blood products, p252; Intracranial haemorrhage, p376; Abdominal sepsis, p350; Bleeding disorders, p396; Haemolysis, p404; Systemic inflammation/multiorgan failure, p484; Vasculitides, p494

Neutropenia

Neutropenia is defined as a neutrophil count $<2 \times 10^9$/l. Life threatening infections may develop below 1×10^9/l and more commonly below 0.5×10^9/l. Absolute numbers of neutrophils are more relevant than percentages as the total white cell count may be either decreased, normal or increased.

Clinical features

- Usually asymptomatic until infection supervenes

Causes

- Systemic inflammation results in margination and aggregation of neutrophils in vital organs, e.g. lung, liver, gut. Predominantly seen in the first 24 h after severe infection or trauma, it is often a precursor of multiple organ dysfunction

- Haemopoietic diseases, e.g. leukaemia, lymphoma, myeloma or as a consequence of chemotherapy or radiation

- Nutritional deficiencies, e.g. folate, vitamin B_{12}, malnutrition

- Adverse drug reaction, e.g. carbimazole, sulphonamides

- Part of aplastic anaemia, e.g. idiopathic, drugs, infection

- Specific infections, e.g. brucellosis, typhoid, viral, protozoal

- Hypersplenism

- Antineutrophil antibodies, e.g. systemic lupus erythematosis

Infections

- Initial infections are with common organisms such as pneumococci, staphylococci and coliforms.

- With recurrent infections or after repeated courses of antibiotics, more unusual and/or antibiotic-resistant organisms may be responsible, e.g. pseudomonas, fungi (particularly *Candida* and *Aspergillus* spp.), pneumocystis, cytomegalovirus, TB.

Management

1. If no diagnosis has been made, urgent investigations including a bone marrow aspiration are indicated.

2. Any implicated drugs should be immediately discontinued.

3. If the neutrophil count falls below 1×10^9/l, the patient should be protectively isolated in a cubicle with strict infection control procedures. Consider laminar flow air conditioning if available.

4. Minimise invasive procedures.

5. Maintain good oral hygiene. Apply topical treatment as necessary, e.g. nystatin mouthwashes for oral fungal infection.

6. Clotrimazole cream for fungal skin infection.

7. Antibiotic therapy

   - For suspected infection use aggressive, parenteral antibiotics (broad spectrum if no organism has been isolated).

   - Have a high index of suspicion for atypical infections such as fungi.

   - Although prophylactic broad-spectrum antibiotics are often prescribed, this encourages antibiotic

resistance. Another alternative is to maintain strict infection control with regular surveillance and to treat infections aggressively as indicated by likely sites and lab results. Avoid uncooked foods, e.g. salads (pseudomonas risk) and bottled pepper (aspergillus).

8. Granulocyte-colony stimulating factor (G-CSF) is frequently given to stimulate a bone marrow response.

9. Neutrophil infusions are short-lived, expensive and often induce a pyrexial response. Their role remains controversial.

See also:

Full blood count, p154; Bacteriology, p158; Antimicrobials, p260; Infection control—general principles, p476; Infection—diagnosis, p480; Infection—treatment, p482

Leukaemia

Such patients may present acutely to an ICU with complications arising from either the disease or the therapy.

Complications arising from the disease

- Decreased resistance to infection
- Hyperviscosity syndrome—drowsiness, coma, focal neurological defects
- Central nervous system involvement
- Anaemia, thrombocytopenia, bleeding tendency, DIC

Complications arising from the therapy

- Tumour lysis syndrome—hyperkalaemia, hyperuricaemia and acute renal failure may follow rapid destruction of a large white cell mass
- Neutropenia and immune compromise with an increased risk of infection
- Anaemia
- Thrombocytopenia leading to spontaneous bleeding, usually from intravascular catheter sites, skin, lung, gut and brain
- Lung fibrosis, e.g. following radiotherapy, bleomycin
- Myocardial failure, e.g. following mitozantrone
- Graft versus host disease (GVHD)—features include mucositis, hepatitis, jaundice, diarrhoea, abdominal pain, rash and pneumonitis

Management

1. Tumour lysis syndrome can be prevented by adequate hydration, maintaining a good diuresis and administering allopurinol. Once established, haemo(dia)filtration and other measures to lower serum potassium levels may be necessary.

2. The raised white cell mass may be reduced by leucophoresis.

3. Frequent blood transfusions to maintain Hb levels >7 g/dl

4. Platelet transfusions are required if counts remain $<10–20 \times 10^9$/l, or if $<50 \times 10^9$/l and remaining symptomatic or undergoing an invasive procedure.

5. Give fresh frozen plasma and other blood products as needed.

6. Neutropenia management, including protective isolation, appropriate antibiotic therapy, ± granulocyte colony stimulating factor.

7. GVHD is managed by supportive treatment and parenteral nutrition. Prostaglandin E_1 and immunosuppression may be helpful.

8. Psychological support for both patient and family is vital.

Respiratory failure

1. Maintenance of gas exchange. Mortality is high (>60%) if mechanical ventilation is necessary. Non-invasive techniques including CPAP and BiPAP can prove highly effective in avoiding the need for intubation.

2. Where possible, treat the cause. Infection (including atypical organisms), fluid overload, ARDS and a pneumonitis/fibrosis secondary to chemo- or radiotherapy should be considered.

See also:

Ventilatory support—indications, p4; Continuous positive airway pressure, p26; Non-invasive respiratory support, p32; Acute respiratory distress syndrome (1), p292; Acute respiratory distress syndrome (2), p294; Heart failure—assessment, p324; Heart failure—management, p326; Acute renal failure—diagnosis, p332; Acute renal failure—management, p334; Diarrhoea, p340; Jaundice, p358; Anaemia, p400; Platelet disorders, p406; Neutropenia, p408; Hyperkalaemia, p420; Infection—diagnosis, p480; Infection—treatment, p482

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Metabolic Disorders

Electrolyte management

A balance must be achieved between electrolyte intake and output. Consider:

- Altered intake
- Impaired renal excretion
- Increased body losses
- Body compartment redistribution (e.g. increased capillary leak, secondary hyperaldosteronism)

As well as Na^+ and K^+, consider Mg^{2+}, Ca^{2+}, Cl^- and PO_4^{3-} balance.

Plasma electrolyte values are poorly reflective of whole body stores; however, excessively high or low plasma levels may induce symptoms and deleterious physiological and metabolic sequelae.

Water balance must also be taken into account; depletion or excess repletion may respectively concentrate or dilute electrolyte levels.

The usual daily requirements of Na^+ and K^+ are 60–80 mmol.

Gravitational peripheral oedema implies increased total body Na^+ and water, though intravascular salt and water depletion may coexist.

Electrolyte losses

•Large nasogastric aspirate, vomiting	Na^+, Cl^-
•Sweating	Na^+, Cl^-
•Polyuria	Na^+, Cl^-, K^+, Mg^{2+}
•Diarrhoea	Na^+, Cl^-, K^+, Mg^{2+}
•Ascitic drainage	Na^+, Cl^-, K^+

Principles of management

1. Establish sources and degree of fluid and electrolyte losses.

2. Assess patient for signs of (i) intravascular fluid depletion—hypotension (e.g. following changes in posture, PEEP, vasodilating drugs) oliguria, increasing metabolic acidosis, thirst, (ii) total body NaCl and water overload—i.e. gravitational oedema.

3. Measure urea, creatinine, osmolality and electrolyte content of plasma and urine.

4. As appropriate, either replace estimated fluid and electrolyte deficit or increase excretion (with diuretics, haemofiltration). For rate of fluid and specific electrolyte replacement see individual sections.

Hypernatraemia

Clinical features

Thirst, lethargy, coma, seizures, muscular tremor and rigidity, and an increased risk of intracranial haemorrhage. Thirst usually occurs when the plasma sodium rises 3–4 mmol/l above normal. Lack of thirst is associated with central nervous system disease.

Treatment

Depends upon the cause and whether total body sodium stores are normal, low or elevated and body water is normal or low.

Rate of correction

- If hyperacute (<12 h), correction can be rapid.

- Otherwise, aim for gradual correction of plasma sodium levels (over 1–3 days), particularly in chronic cases (>2 days' duration), to avoid cerebral oedema through sudden lowering of osmolality. A rate of plasma sodium lowering <0.7 mmol/h has been suggested.

Hypovolaemia

- If hypovolaemia is accompanied by haemodynamic alterations, use colloid initially to restore the circulation. Otherwise, use isotonic saline.

- Artificial colloid solutions consist of hydroxyethyl starches (e.g. Hespan, EloHAES) or gelatins (e.g. Gelofusin, Haemaccel) dissolved in isotonic saline.

Normal total body Na (water loss)

- Water replacement either PO (addition to enteral feed) or as 5% glucose IV. Up to 5l/day may be necessary.

- If cranial diabetes insipidus (CDI): restrict salt and give thiazide diuretics. Complete CDI will require desmopressin (10μg bd intranasally or 1–2μg bd IV) whereas partial CDI may require desmopressin but often responds to drugs that increase the rate of ADH secretion or end-organ responsiveness to ADH, e.g. chlorpropamide, hydrochlorthiazide

- If nephrogenic DI: manage by a low salt diet and thiazides. High dose desmopressin may be effective. Consider removal of causative agents, e.g. lithium, demeclocycline.

Low total body Na (Na and water losses)

- Treat hyperosmolar non-ketotic diabetic crisis, uraemia as appropriate.

- Otherwise consider 0.9% saline or hypotonic (0.45%) saline. Up to 5 l/day may be needed.

Increased total body Na (Na gain)

- Water replacement either PO (addition to enteral feed) or as 5% glucose IV. Up to 5l/day may be necessary.

- In addition, furosemide 10–20 mg IV prn may be necessary.

Causes of hypernatraemia

Type	Aetiology	Urine
Low total body Na	Renal losses: diuretic excess, osmotic diuresis (glucose, urea, mannitol)	$[Na^+]$ >20 mmol/l iso- or hypotonic
Extra-renal losses: excess sweating		$[Na^+]$ <10 mmol/l hypertonic
Normal total body Na	Renal losses: diabetes insipidus	$[Na^+]$ variable hypo-, iso- or hypertonic
Extra-renal losses: respiratory and renal insensible losses		$[Na^+]$ variable hypertonic
Increased total body Na	Conn's syndrome, Cushing's syndrome, excess NaCl, hypertonic $NaHCO_3$	$[Na^+]$ >20 mmol/l iso- or hypertonic

See also:

Haemo(dia)filtration (1), p62; Haemo(dia)filtration (2), p64; Enteral nutrition, p80; Parenteral nutrition, p82; Electrolytes

$(Na^+, K^+, Cl^-, HCO_3^-)$

, p146; Urinalysis, p166; Crystalloids, p176; Colloids, p180; Diuretics, p212; Electrolyte management, p414; Diabetic ketoacidosis, p442; Hyperosmolar diabetic emergencies, p444

Hyponatraemia

Clinical features

Nausea, vomiting, headache, fatigue, weakness, muscular twitching, obtundation, psychosis, seizures and coma. Symptoms depend on the rate as well as the magnitude of fall in the plasma $[Na^+]$.

Treatment

Rate and degree of correction

- In chronic hyponatraemia correction should not exceed 0.5 mmol/l/h in the first 24 h and 0.3 mmol/l/h thereafter.

- In acute hyponatraemia the ideal rate of correction is controversial though elevations in plasma Na^+ can be faster, but <20 mmol/l/day.

- A plasma Na^+ of 125–130 mmol/l is a reasonable target for initial correction of both acute and chronic states. Attempts to achieve normo- or hypernatraemia rapidly should be avoided.

- Neurological complications, e.g. central pontine myelinolysis, are related to the degree of correction and (in chronic hyponatraemia) the rate. Premenopausal women are more prone to these complications.

Extracellular fluid (ECF) volume excess

- If symptomatic (e.g. seizures, agitation), and not oedematous, 100 ml aliquots of hypertonic (1.8%) saline can be given, checking plasma levels every 2–3 h.

- If symptomatic and oedematous, consider furosemide (10–20 mg IV bolus prn), mannitol (0.5g/kg IV over 15–20 min), and replacement of urinary sodium losses with aliquots of hypertonic saline. Check plasma levels every 2–3 h. Haemofiltration or dialysis may be necessary if renal failure is established.

- If not symptomatic, restrict water to 1–1.5 l/day. If hyponatraemia persists, consider inappropriate ADH (SIADH) secretion.

- If SIADH likely, give isotonic saline and consider demeclocycline.

- If SIADH unlikely, consider furosemide (10–20 mg IV bolus prn), mannitol (0.5 g/kg IV over 15–20 min), and replacement of urinary sodium losses with aliquots of hypertonic saline.

- Check plasma levels regularly. Haemofiltration or dialysis may be necessary if renal failure is established.

Extracellular fluid volume (ECF) depletion

- If symptomatic (e.g. seizures, agitation), give isotonic (0.9%) saline. Consider hypertonic (1.8%) saline.

- If not symptomatic, give isotonic (0.9%) saline.

General points

- Equations that calculate excess water are unreliable. It is safer to perform frequent estimations of plasma sodium levels.

- Hypertonic saline may be dangerous in the elderly and those with impaired cardiac function. An alternative is to use furosemide with replacement of urinary sodium (and potassium) losses each 2–3 h. Thereafter, simple water restriction is usually sufficient.

- Many patients achieve normonatraemia by spontaneous water diuresis.

- Use isotonic solutions for reconstituting drugs, parenteral nutrition, etc.

- Hyponatraemia may intensify the cardiac effects of hyperkalaemia.

- A true hyponatraemia may occur with a normal osmolality in the presence of abnormal solutes e.g. ethanol, ethylene glycol, glucose.

Causes of hyponatraemia

Type	Aetiology	Urine [Na$^+$]
ECF volume depletion	Renal losses: diuretic excess, osmotic diuresis (glucose, urea, mannitol), renal tubular acidosis, salt-losing nephritis, mineralocorticoid deficiency	>20 mmol/l
Extra-renal losses: vomiting, diarrhoea, burns, pancreatitis		<10 mmol/l
Modest ECF volume excess (no oedema)	water intoxication (NB post-operative, TURP syndrome), inappropriate ADH secretion, hypothyroidism, drugs (e.g. carbamazepine, chlorpropamide), glucocorticoid deficiency, pain, emotion.	>20 mmol/l
acute and chronic renal failure		>20 mmol/l
ECF volume excess (oedema)	nephrotic syndrome, cirrhosis, heart failure	<10 mmol/l

Causes of inappropriate ADH secretion

- Neoplasm, e.g. lung, pancreas, lymphoma

- Most pulmonary lesions

- Most central nervous system lesions

- Surgical and emotional stress

- Glucocorticoid and thyroid deficiency

- Idiopathic

- Drugs, e.g. chlorpropamide, carbamazepine, narcotics

See also:

Haemo(dia)filtration (1), p62; Haemo(dia)filtration (2), p64; Enteral nutrition, p80; Parenteral nutrition, p82; Electrolytes

$(Na^+, K^+, Cl^-, HCO_3^-)$

, p146; Urinalysis, p166; Crystalloids, p176; Colloids, p180; Diuretics, p212; Acute renal failure—diagnosis, p332; Acute renal failure—management, p334; Electrolyte management, p414; Diabetic ketoacidosis, p442; Hyperosmolar diabetic emergencies, p444

Hyperkalaemia

Plasma potassium depends on the balance between intake, excretion and the distribution of potassium across cell membranes. Excretion is normally controlled by the kidneys.

Causes

- Reduced renal excretion (e.g. chronic renal failure, adrenal insufficiency, diabetes, potassium sparing diuretics)
- Intracellular potassium release (e.g. acidosis, rapid transfusion of old blood, cell lysis including rhabdomyolysis, haemolysis and tumour lysis, K^+ channel openers (nicorandil))
- Potassium poisoning

Clinical features

Hyperkalaemia may cause dangerous arrhythmias including cardiac arrest. Arrhythmias are more closely related to the rate of rise of potassium than the absolute level. Clinical features such as paraesthesiae and areflexic weakness are not clearly related to the degree of hyperkalaemia but usually occur after ECG changes (tall 'T' waves, flat 'P' waves, prolonged PR interval and wide QRS).

Management

Potassium restriction is needed for all cases and haemodiafiltration or haemodialysis may be needed for resistant cases.

Cardiac arrest associated with hyperkalaemia

Sodium bicarbonate (8.4%) 50–100 ml should be given in addition to standard CPR and other treatment detailed below.

Potassium >7 mmol/l

Calcium chloride (10%) 10 ml should be given urgently in addition to treatment detailed below. Although calcium chloride does not reduce the plasma potassium, it stabilises the myocardium against arrhythmias.

Clinical features of hyperkalaemia or potassium >6 mmol/l with ECG changes

Glucose (50 ml 50%) and soluble insulin (10 iu) should be given IV over 20 min. Blood glucose should be monitored every 15 min and more glucose given if necessary. In addition, calcium resonium 15 g qds PO or 30 g bd PR can be considered.

See also:

Haemo(dia)filtration (1), p62; Haemo(dia)filtration (2), p64; Enteral nutrition, p80; Parenteral nutrition, p82; Electrolytes

$(Na^+, K^+, Cl^-, HCO_3^-)$

, p146; Urinalysis, p166; Crystalloids, p176; Diuretics, p212; Cardiac arrest, p272; Bradyarrhythmias, p318; Acute renal failure—diagnosis, p332; Acute renal failure—management, p334; Electrolyte management, p414; Rhabdomyolysis, p528

Hypokalaemia

Plasma potassium depends on the balance between intake, excretion and the distribution of potassium across cell membranes. Excretion is normally controlled by the kidneys.

Causes

- Inadequate intake
- Gastrointestinal losses (e.g. vomiting, diarrhoea, fistula losses)
- Renal losses (e.g. diabetic ketoacidosis, Conn's syndrome, secondary hyperaldosteronism, Cushing's syndrome, renal tubular acidosis, metabolic alkalosis, hypomagnesaemia, drugs including diuretics, steroids, theophyllines)
- Haemofiltration losses
- Potassium transfer into cells (e.g. acute alkalosis, glucose infusion, insulin treatment, familial periodic paralysis)

Clinical features

- Arrhythmias (SVT, VT and Torsades de Pointes)
- ECG changes (ST depression, 'T' wave flattening, 'U' waves)
- Metabolic alkalosis
- Constipation
- Ileus
- Weakness

Management

- Wherever possible, the cause of potassium loss should be treated.

- Potassium replacement should be intravenous with ECG monitoring when there is a clinically significant arrhythmia (20 mmol over 30 min, repeated according to levels).

- Slower intravenous replacement (20 mmol over 1 h) should be used where there are clinical features without arrhythmias.

- Oral supplementation (to a total intake of 80–120 mmol/day, including nutritional input) can be given where there are no clinical features.

See also:

Enteral nutrition, p80; Parenteral nutrition, p82; Electrolytes
$(Na^+, K^+, Cl^-, HCO_3^-)$
, p146; Urinalysis, p166; Crystalloids, p176; Diuretics, p212; Steroids, p262; Cardiac arrest, p272; Tachyarrhythmias, p316; Electrolyte management, p414; Metabolic alkalosis, p436; Diabetic ketoacidosis, p442; Post-operative intensive care, p534

Hypomagnesaemia

Causes

- Excess loss, e.g. diuretics, other causes of polyuria (including poorly controlled diabetes mellitus), severe diarrhoea, prolonged vomiting, large nasogastric aspirates

- Inadequate intake, e.g. starvation, parenteral nutrition, alcoholism, malabsorption syndromes

Clinical features

Magnesium is primarily an intracellular ion involved in the production and utilisation of energy stores and in the mediation of nerve transmission. Low plasma levels, which do not necessarily reflect either intracellular or whole body stores, may thus be associated with features related to these functions:

- Confusion, irritability

- Seizures

- Muscle weakness, lethargy

- Arrhythmias

- Symptoms related to hypocalcaemia and hypokalaemia which are resistant to calcium and potassium supplementation respectively

Normal plasma levels range from 0.7–1.0 mmol/l; severe symptoms do not usually occur until levels drop below 0.5 mmol/l.

Management

- Where possible, identify and treat the cause.

- For severe, symptomatic hypomagnesaemia, 10 mmol of magnesium sulphate can be given IV over 3–5 min. This can be repeated once or twice as necessary.

- In less acute situations or for asymptomatic hypomagnesaemia, 10–20 mmol $MgSO_4$ solution can be given over 1–2 h and repeated as necessary, or according to repeat plasma levels.

- A continuous IV infusion (e.g. 3–5 mmol $MgSO_4$ solution/h) can be given; however, this is usually reserved for therapeutic indications where supranormal plasma levels (1.5–2 mmol/l) of magnesium are sought, e.g. treatment of supraventricular and ventricular arrhythmias, pre-eclampsia and eclampsia, bronchospasm.

- Oral magnesium sulphate has a laxative effect and may cause severe diarrhoea.

- High plasma levels of magnesium may develop in renal failure; caution should be applied when administering IV magnesium.

See also:

Enteral nutrition, p80; Parenteral nutrition, p82; Calcium, magnesium and phosphate, p148; Diuretics, p212; Asthma—general management, p296; Tachyarrhythmias, p316; Electrolyte management, p414; Generalised seizures, p372; Pre-eclampsia and eclampsia, p538

Hypercalcaemia

Causes

- Malignancy (e.g. myeloma, bony metastatic disease, hypernephroma)
- Hyperparathyroidism
- Sarcoidosis
- Excess intake of calcium, vitamin A or D
- Drugs, e.g. thiazides, lithium
- Immobilisation
- Rarely, thyrotoxicosis, Addison's disease

Clinical features

Usually become apparent when total (ionised and un-ionised) plasma levels >3.5 mmol/l (normal range 2.2–2.6 mmol/l). Symptoms depend on the patient's age, the duration and rate of increase of plasma calcium, and the presence of concurrent medical conditions.

- Nausea, vomiting, weight loss, pruritus
- Muscle weakness, fatigue, lethargy
- Depression, mania, psychosis
- Drowsiness, coma
- Abdominal pain, constipation
- Acute pancreatitis
- Peptic ulceration
- Polyuria, renal calculi, renal failure
- Arrhythmias

Management

1. Identify and treat cause where possible.
2. Carefully monitor haemodynamic variables, urine output, and ECG morphology with frequent estimations of plasma Ca^{2+}, PO_4^{3-}, Mg^{2+}, Na^+ and K^+.
3. Intravascular volume repletion—this inhibits proximal tubular reabsorption of calcium and often lowers the plasma calcium by 0.4–0.6 mmol/l. It should precede diuretics or any other therapy. Either colloid or 0.9% saline should be used, depending on the presence of hypovolaemia-related features.
4. Calciuresis—after adequate intravascular volume repletion, a forced diuresis with furosemide plus 0.9% saline (6–8 l/day) may be attempted. An effect is usually seen within 12 h. Loop diuretics inhibit calcium reabsorption in the ascending limb of the loop of Henlé. More aggressive furosemide regimens can be attempted but can potentially result in complications. Thiazides should not be used as tubular reabsorption may be reduced and hypercalcaemia worsened.
5. Dialysis/haemofiltration—may be indicated at an early stage if the patient is in established oligo-anuric renal failure ± fluid overloaded.
6. Steroids can be effective for hypercalcaemia related to haematological cancers (lymphoma, myeloma), vitamin D overdose and sarcoidosis.
7. Calcitonin has the most rapid onset of action with a nadir often reached within 12–24 h. Its action is usually short-lived and rebound hypercalcaemia may occur. It generally does not drop the plasma level more than 0.5 mmol/l.
8. Biphosphonates (e.g. pamidronate) and IV phosphate should only be given after specialist advice is taken in view of their toxicity and potential complications.

Drug dosage

Diuretics	Furosemide 10–40 mg IV 2–4 h (may be increased to 80–100 mg IV every 1–2 h)
Steroids	Hydrocortisone 100 mg qds IV or prednisolone 40–60 mg PO for 3–5 days
Pamidronate	15–60 mg slow IV bolus
Calcitonin	3–4 U/kg IV followed by 4 U/kg SC bd

See also:

Calcium, magnesium and phosphate, p148; Diuretics, p212; Steroids, p262; Acute renal failure—diagnosis, p332; Acute renal failure—management, p334; Pancreatitis, p354; Electrolyte management, p414; Diabetic ketoacidosis, p442; Thyroid emergencies, p446; Hypoadrenal crisis, p448

Hypocalcaemia

Causes

- Associated with hyperphosphataemia:
    - Renal failure
    - Rhabdomyolysis
    - Hypoparathyroidism (including surgery), pseudohypoparathyroidism
- Associated with low/normal phosphate:
    - Critical illness including sepsis, burns
    - Hypomagnesaemia
    - Pancreatitis
    - Osteomalacia
    - Over-hydration
- Massive blood transfusion (citrate-binding)
- Hyperventilation and the resulting respiratory alkalosis may reducethe ionised plasma calcium fraction and induce clinical features of hypocalcaemia

Clinical features

These usually appear when total plasma calcium levels <2 mmol/l and the ionised fraction is <0.8 mmol/l.

- Tetany (including carpopedal spasm)
- Muscular weakness
- Hypotension
- Perioral and peripheral parasthesiae
- Chvostek & Trousseau's signs
- Prolonged QT interval
- Seizures

Management

1. If respiratory alkalosis is present, adjust ventilator settings or, if spontaneously hyperventilating and agitated, calm ± sedate. Rebreathing into a bag may be beneficial.
2. If symptomatic, give 5–10 ml 10% calcium chloride solution over 2–5 min. Repeat as necessary.
3. Dorrect hypomagnesaemia or hypokalaemia if present.
4. If asymptomatic and in renal failure or hypoparathyroid, consider enteral/parenteral calcium supplementation and vitamin D analogues.
5. If hypotensive or cardiac output is decreased following administration of a calcium antagonist, give 5–10 ml 10% calcium chloride solution over 2–5 min.

Hypophosphataemia

Causes

- Critical illness

- Inadequate intake

- Loop diuretic therapy (including low dose dopamine)

- Parenteral nutrition—levels fall rapidly during high dose intravenous glucose therapy, especially with insulin

- Alcoholism

- Hyperparathyroidism

Clinical effects

Hypophosphataemia is associated with muscle weakness; however, this is rarely clinically apparent, even in patients with severe hypophosphataemia where plasma levels may drop <0.1 mmol/l.

Treatment

Phosphate supplements (5–10 mmol) should be given by intravenous infusion over 6 h and repeated according to the plasma phosphate level.

General acid–base management

Increased intake, altered production or impaired/excessive excretion of acid or base leads to derangements in blood pH. Augmented renal excretion of H^+ ions may result from hypokalaemia. With time, respiratory and renal adjustments correct the pH towards normality by altering the plasma level of PCO_2 or HCO_3^-.

Increased intake

- Acid: aspirin overdose

- Base: $NaHCO_3$ administration, antacid abuse, buffered replacement fluid (haemofiltration)

Altered production

- Increased acid production: lactic acidosis (usually secondary to hypoperfusion), diabetic ketoacidosis

- Increased base production: chronic hypercapnic respiratory failure, permissive hypercapnia

- Decreased base production: chronic hyperventilation

Altered excretion

- Increased acid loss: vomiting, large gastric aspirates, diuretics, hyperaldosteronism, corticosteroids

- Increased base loss: diarrhoea, small bowel fistula, urethroenterostomy, proximal renal tubular acidosis

- Decreased acid loss: renal failure, distal renal tubular acidosis, acetazolamide

- Decreased base loss: chronic hypercapnic respiratory failure, permissive hypercapnia

Principles of management

- Correct (where possible) the abnormality, e.g. hypoperfusion

- Consider addition of 'substrate' and physiological corrective functions

- NaCl infusion for vomiting-induced alkalosis; insulin, Na^+ and K^+ in diabetic ketoacidosis

- Correct pH in specific circumstances only, e.g. $NaHCO_3$ in renal failure

See also:

Blood gas analysis, p100; Lactate, p170; Sodium bicarbonate, p178; Respiratory failure, p282; Chronic airflow limitation, p286; Metabolic acidosis, p434; Metaboloic alkalosis, p436

Metabolic acidosis

A subnormal arterial blood pH with a base deficit >2 mmol/l. Outcome in critically ill patients has been linked to the severity and duration of metabolic acidosis and hyperlactataemia.

Causes

- Tissue hypoperfusion, e.g. heart failure, hypovolaemia, sepsis. The anion gap is related to production of lactic and other organic acids. Anaerobic metabolism contributes in part to this metabolic acidosis although other cellular mechanisms are involved.

- Tissue necrosis, e.g. bowel, muscle.

- Hyperchloraemia, e.g. excessive saline infusion.

- Ketoacidosis—high levels of β-hydroxybutyrate and acetoacetate related to uncontrolled diabetes mellitus, starvation and alcoholism.

- Renal failure—accumulation of organic acids, e.g. sulphuric.

- Drugs—in particular, aspirin (salicylic acid) overdose, acetazolamide (carbonic anhydrase inhibition), ammonium chloride. Vasopressor agents may be implicated, possibly by inducing regional ischaemia or, in the case of epinephrine, accelerated glycolysis.

- Ingestion of poisons, e.g. paraldehyde, ethylene glycol, methanol.

- Bicarbonate loss, e.g. severe diarrhoea, small bowel fistulae, large ileostomy losses.

- Type B lactic acidosis—no evidence of tissue hypoperfusion.

Causes of type B lactic acidosis

Acute infection

Diabetes mellitus

Drugs, e.g. phenformin, metformin, alcohols

Glucose-6-phosphatase deficiency

Haematological malignancy

Hepatic failure

Pancreatitis

Renal failure

Short bowel syndrome (D-lactate)

Thiamine deficiency

Clinical features

- Dyspnoea

- Haemodynamic instability

- A rapidly increasing metabolic acidosis (over minutes to hours) is not due to renal failure. Other causes, particularly severe tissue hypoperfusion, sepsis or tissue necrosis should be suspected when there is associated systemic deterioration

Management

1. The underlying cause should be identified and treated where possible rather than administering alkali or manipulating minute volume to normalise the arterial pH.

2. Urgent haemo(dia)filtration may be necessary if oliguria persists.

3. Reversal of the metabolic acidosis (other than simple buffering with bicarbonate) is generally an indication of successful therapy. An increasing base deficit suggests that the therapeutic manoeuvres in operation are either inadequate or wrong.

4. The benefits of buffers such as Carbicarb and THAM (tris-hydroxy-methyl-aminomethane) remain unproved and are not generally available.

Metabolic alkalosis

- A supranormal arterial blood pH with a base excess >2 mmol/l caused either by loss of (non-carbonic) acid or gain of base. As the kidney is usually efficient at excreting large quantities of bicarbonate, persistence of a metabolic alkalosis usually depends on either chronic renal failure or a diminished extracellular fluid volume with severe depletion of K^+.

- The patient is usually asymptomatic though, if spontaneously breathing, will hypoventilate.

- A metabolic alkalosis will cause a left shift of the oxyhaemoglobin curve, reducing oxygen availability to the tissues.

Causes

- Loss of total body fluid, Na^+, Cl^+, K^+ usually due to:
  - diuretics
  - large nasogastric aspirates, vomiting
- Secondary hyperaldosteronism with potassium depletion
- Use of haemofiltration replacement fluid containing excess buffer (e.g. lactate)
- Renal compensation for chronic hypercapnia. This can develop within 1–2 weeks. Although more apparent when the patient hyperventilates, or is hyperventilated to normocapnia, an overcompensated metabolic alkalosis can occasionally be seen in the chronic state (i.e. a raised pH in an otherwise stable long term hypercapnic patient)
- Excess administration of bicarbonate
- Excess administration of citrate (large blood transfusion)
- Drugs, including laxative abuse, corticosteroids
- Rarely, Cushing's, Conn's, Bartter's syndrome

Management

1. Replacement of fluid, sodium, chloride (i.e. give 0.9% saline) and potassium losses are often sufficient to restore acid–base balance.

2. With distal renal causes related to hyperaldosteronism, addition of spironolactone (or potassium canrenoate) can be considered.

3. Active treatment is rarely necessary. If so, give ammonium chloride 5 g tds PO. Hydrochloric acid has been used on occasion for severe metabolic alkalosis (pH >7.7). It should be given via a central vein in a concentration of 1 mmol HCl per ml water at a rate not exceeding 1 mmol/kg/h.

4. Compensation for a long-standing respiratory acidosis, followed by correction of that acidosis, e.g. with mechanical ventilation, will lead to an uncompensated metabolic alkalosis. This usually corrects with time though treatments such as acetazolamide can be considered. Mechanical 'hypoventilation', i.e. maintaining hypercapnia, can also be considered.

See also:

Hypoglycaemia

Causes

- Inadequate intake of carbohydrate
- Excess insulin or sulphonylurea
- Liver failure with depletion of glycogen stores
- Alcohol
- Hypoadrenalism (including Addison's disease), hypopituitarism
- Quinine, aspirin

Clincal features

- Nausea, vomiting

- Increased sympathetic activity, e.g. sweating, tachycardia

- Altered behaviour and conscious level

- Seizures, focal neurological signs

Management

1. Monitor carefully with regular bedside estimations. The frequency should be increased in conditions known to precipitate hypoglycaemia, e.g. insulin infusion, liver failure, quinine treatment of malaria.

2. Administer 25 ml 50% glucose solution if the blood glucose is:

   - ≤ 3 mmol/l or

   - ≤ 4 mmol/l and the patient is symptomatic or

   - Within the normal range but the patient is symptomatic (usually long-standing poorly controlled diabetics)

   Repeat as necessary every few minutes until symptoms abate and the blood glucose level has normalised.

3. If the blood glucose is 3–4 mmol/l and the patient is non-symptomatic, either reduce the rate of insulin infusion (if present), or increase calorie intake (enterally or parenterally). In insulin dependent diabetes mellitus, the insulin should continue with adequate glucose intake.

4. A continuous parenteral infusion of 10%, 20% or 50% glucose solution varying from 10–100 ml/h may be required, depending on the degree of continuing hypoglycaemia and the patient's fluid balance/urine output. 5% glucose solution only contains 20Cal/100 ml and should not be used to prevent or treat hypoglycaemia.

5. In the rare instance of no venous access, hypoglycaemia may be temporarily reversed by glucagon 1 mg given either IM or SC.

6. Continuing hypoglycaemia in the face of adequate treatment and lack of symptoms should be confirmed with a formal laboratory blood sugar estimation to exclude malfunctioning of the bedside testing equipment.

See also:

Hyperglycaemia

Causes

- A common occurrence in critically ill patients due to a combination of impaired glucose tolerance, insulin resistance, high circulating levels of endogenous catecholamines and corticosteroids, and regular administration of such drugs which antagonise the effect of insulin

- Pancreatitis resulting in islet cell damage

Clinical features

None in the short term, other than polyuria from the osmotic diuresis. The patient may complain of thirst or show signs of hypovolaemia if fluid balance is allowed to become too negative.

Metabolic effects

Relative lack of insulin prevents cellular glucose uptake and utilisation resulting in:

- Increased lipolysis

- Altered cellular metabolism

- Increased risk of infection (decreased neutrophil action)

Prognostic significance

Strict maintenance of glycaemic control (approx. 4–7 mmol/l) resulted in significant outcome improvement in a surgical ICU population. Whether this is related to prevention of hyperglycaemia and/or an effect related to additional administration of insulin remains uncertain.

Management

1. Treatment should be given if blood glucose elevations persist (>7–8 mmol/l).

2. A short-acting insulin infusion (e.g. actrapid) should be used and titrated to maintain normoglycaemia (4–7

mmol/l). Usually 1–4Units/h are required though may need to be much higher in diabetics who become critically ill. Regular bedside monitoring of blood sugar should be performed; this should be undertaken hourly if unstable.

3. Oral hypoglycaemic agents should be generally avoided in the ICU patient because of their prolonged duration of action and unpredictable absorption.

Key trial

Van den Berghe G, et al. Intensive insulin therapy in critically ill patients. N Engl J Med 2001; 345:1359–67

Diabetic ketoacidosis

This may occur *de novo* in a previously undiagnosed diabetic or follow an acute insult (e.g. infection) in a known diabetic patient.

Clinical features

- Excess fat metabolism to fatty acids with ketone production
- An osmotic diuresis with large losses of fluid (up to 6–10l), sodium (400–800 mmol), potassium (250–800 mmol) and magnesium

Symptoms result from hypovolaemia, metabolic acidosis and electrolyte imbalance with polyuria. Hyperventilation is a prominent feature.

Coma need not necessarily be present for life to be threatened.

Plasma amylase commonly exceeds 1000U/l but does not indicate pancreatitis. If suspected, perform an abdominal ultrasound.

Monitoring

Adequate invasive monitoring is essential, particularly if the patient has circulatory instability or cardiac dysfunction. Urine output, blood gases and plasma electrolytes should also be monitored frequently.

Fluid and electrolyte management

1. Fluid and electrolyte repletion should be tailored to individual needs. Traditional regimens (e.g. 3–4 l within the first 3–4 h) increase the risk of cerebral oedema, cardiac and/or renal failure.

2. Colloid fluid challenges should be given to restore the circulating blood volume in tissue hypoperfusion.

3. Fluid replacement with 0.9% saline should be given at a rate of 200 ml/h until the salt and water debt has been replenished.

4. Hypotonic (0.45%) saline resuscitation may be appropriate in the non-shocked patient if the plasma sodium is rising rapidly (shift of water and potassium into cells and sodium out).

5. Substitute 5% glucose solution (100–200 ml/h) after replacing the sodium debt; usually when the blood sugar falls to <10 mmol/l.

6. Carefully monitor K^+ replacement. Both acidosis and excessive K^+ administration cause hyperkalaemia while fluid and insulin will produce hypokalaemia. Check levels frequently to maintain normokalemia. Infusion of 10–40 mmol/h KCl will be needed.

7. Carefully monitor magnesium replacement: 3–5 mmol/h $MgSO_4$ is usually sufficient.

Hyperglycaemia

Correct slowly at a rate of 2–4 mmol/h by adjusting the short acting insulin infusion (usually 1–5U/h). Monitor blood glucose hourly. Continue IV insulin (with glucose after achieving normoglycaemia) until heavy ketonuria has disappeared and the base deficit normalised.

Other aspects of managing ketoacidosis

1. Seek a precipitating cause and treat as indicated. Approximately 50% are related to underlying disease, e.g. sepsis, myocardial infarction, stroke, infective gastroenteritis.

2. Only give antibiotics for proved or highly suspected infection.

3. Abdominal pain should not be dismissed as part of the syndrome.

4. A nasogastric tube should be inserted, as gastric emptying is often delayed and acute gastric dilatation is common.

5. Avoid bicarbonate, even for severe acidosis (pH <7.0). It causes an increased intracellular acidosis and

depressed respiration due to a relative CSF alkalosis. Sodium overload may also occur.

6. Low molecular weight heparin 5000U SC od is indicated in immobile or comatose patients.

See also:

Central venous catheter—use, p114; Central venous catheter—insertion, p116; Electrolytes $(Na^+, K^+, Cl^-, HCO_3^-)$, p146; Bacteriology, p158; Urinalysis, p166; Crystalloids, p176; Fluid challenge, p274; Anticoagulants, p248; Antimicrobials, p260; Oliguria, p330; Vomiting/gastric stasis, p338; Abdominal sepsis, p350; Hyperkalaemia, p420; Hypokalaemia, p422; Hypomagnesaemia, p424; Hyperglycaemia, p440; Metabolic acidosis, p434; Infection—diagnosis, p480; Infection—treatment, p482

Hyperosmolar diabetic emergencies

This is more common in elderly, non-insulin dependent diabetics though can present *de novo* in young adults.

Precipitating factors are similar to ketoacidosis, e.g. sepsis, myocardial infarction

Clinical features

- Fluid depletion is greater, blood glucose levels often higher, coma more frequent and mortality much higher than in diabetic ketoacidosis.

- Confusion, agitation and drowsiness that may persist for 1–2 weeks.

- A metabolic acidosis may be present but is not usually profound; ketoacidosis is not a major feature.

- Hyperosmolality may predispose to thrombotic events; this is the major cause of mortality. Severe hyperosmolality does not always occur.

- Focal neurological signs and disseminated intravascular coagulation are occasionally recognised.

Management

As for diabetic ketoacidosis; however:

1. Unless the patient shows signs of hypovolaemia and tissue hypoperfusion, in which case colloid challenges should be given for prompt resuscitation, fluid replacement should be more gradual as the risk of cerebral oedema is higher. This can be with either 0.9% saline or, if the plasma sodium is high, 0.45% saline at a rate of 100–200 ml/h.

2. The plasma sodium rises with treatment, even with 0.45% saline, and can often increase in the first few days to 160–170 mmol/l before gradually declining thereafter. Aim to correct slowly.

3. Serum phosphate and magnesium levels fall rapidly with this condition; replacement may be needed as guided by frequently taken plasma levels.

4. Patients may be hypersensitive to insulin and require lower doses.

5. Unless otherwise contraindicated, these patients should be fully heparinised until full recovery (which may take ≥5 days).

See also:

Electrolytes $(Na^+, K^+, Cl^-, HCO_3^-)$, p146; Bacteriology, p158; Urinalysis, p166; Crystalloids, p176; Anticoagulants, p248; Antimicrobials, p260; Fluid challenge, p274; Oliguria, p330; Vomiting/gastric stasis, p338; Abdominal sepsis, p350; Hypernatraemia, p416; Hyponatraemia, p418; Hyperkalaemia, p420; Hypokalaemia, p422; Hypomagnesaemia, p424; Hypophosphataemia, p430; Hyperglycaemia, p440; Diabetic ketoacidosis, p442; Infection—diagnosis, p480; Infection—treatment, p482

Thyroid emergencies

Thyrotoxic crisis

Presents as an exacerbation of the clinical features of hyperthyroidism (e.g. pyrexia, hyperdynamic circulation, heart failure, confusion). There is usually a precipitating factor such as infection, surgery, ketoacidosis, myocardial infarction or childbirth. It may present with exhaustion in the elderly with few features of hyperthyroidism. The diagnosis is confirmed by standard thyroid function tests.

Management

- Pyrexia should be controlled by surface cooling (avoid aspirin which displaces thyroxine from plasma proteins).

- Catecholamine effects should be reduced by β blockade (e.g. propranolol 1–5 mg IV then 20–80 mg qds PO). These should be used with caution if there is acute heart failure.

- Blockade of thyroxine synthesis is achieved by potassium iodide 200–600 mg IV over 2 h then 2 g/day PO and carbimazole 60–120 mg/day PO.

- Blockade of peripheral T4 to T3 conversion is achieved by dexamethasone 2 mg qds IV.

- Careful fluid and electrolyte management is essential.

Myxoedema coma

Presents as an exacerbation of the features of hypothyroidism (e.g. hypothermia, coma, bradycardia, metabolic and respiratory acidosis, anaemia). There may be a precipitating factor (e.g. cold, infection, surgery, myocardial infarction, CVA, central nervous system depressant drugs). Diagnosis is confirmed by thyroid function tests.

Management

- Treatment of the complications of severe hypothyroidism (e.g. hypotension, heart failure, hypothermia, bradycardia, seizures) is more important than thyroid hormone replacement.

- Thyroxine replacement should be with low doses (0.1–0.2 mg PO or PR unless ischaemic heart disease is possible, then start at 0.25 mg).

- There are no definite advantages to using T3 replacement, high dose replacement regimens or intravenous treatment.

- Steroids (hydrocortisone 100 mg qds IV) should be given since coexisting hypoadrenalism is masked by myxoedema.

Sick euthyroid/low T3 syndrome

This is a frequent complication of critical illness with low T3 and T4 and high reverse T3 (rT3) levels. These correlate with the severity of disease and a poor outcome. There is both reduced TSH secretion and altered peripheral thyroid metabolism. A trial of thyroxine administration in critically ill patients produced a negative outcome although those suffering from the sick euthyroid syndrome were not identified. Treatment of this syndrome thus remains unknown.

See also:

Hypoadrenal crisis

Clinical features

Primary hypoadrenalism

- Glucocorticoid deficiency (e.g. weakness, vomiting, diarrhoea, abdominal pain, hypoglycaemia)

- Mineralocorticoid deficiency (e.g. dehydration, hyponatraemia, weight loss, postural hypotension, hyperkalaemia)

- Skin pigmentation due to ACTH excess

Secondary hypoadrenalism

- May be due to critical illness, steroid withdrawal after 2 weeks' treatment, hypopituitarism or etomidate use

- No skin pigmentation

- Features of mineralocorticoid deficiency may be absent

Diagnosis

Diagnosis is confirmed by plasma cortisol, ACTH levels and a negative Tetracosactrin (ACTH analogue) test, although treatment should begin on clinical suspicion. A dose of 250µg IV should produce a >200 nmol/l rise in plasma cortisol. In primary hypoadrenalism levels remain below 600 nmol/l. However, basline levels may be normal or elevated in the relative adrenal deficiency seen in sepsis and other critical illnesses. Dexamethasone may be used for steroid replacement for 48 h before an ACTH test is performed since other steroid treatments are detected in the plasma cortisol assay.

Management

- Salt and water deficiency should be corrected urgently. Initial fluid replacement should be with colloid if there is hypotension, or evidence of poor tissue perfusion. Otherwise 4–5l/day 0.9% saline will be needed for several days.

- Fluid management should be carefully monitored to ensure adequate replacement without fluid overload.

- Glucocorticoid replacement should be with hydrocortisone 50–100 mg tds IV on day 1 then 20–50 mg tds on days 2–3. Hydrocortisone may be changed to equivalent doses of dexamethasone before the ACTH test has been performed.

- The relative hypoadrenalism related to sepsis can be treated with hydrocortisone 50 mg qds for 7 days, and then a reducing dose over the next 5–7 days. Studies have shown more rapid resolution of shock and an improved outcome in those showing a suboptimal response to synthetic ACTH, despite raised baseline levels.

See also:

🟢 Ovid: Oxford Handbook of Critical Care

Poisoning

Poisoning—general principles

Poisoning should be considered in patients presenting with altered consciousness, respiratory or cardiovascular depression, vomiting, hypothermia or seizures. The history usually makes diagnosis obvious although clinical signs may be confused due to ingestion of multiple poisons or absent if effects are delayed. It should be remembered that poisons may enter the body via routes other than ingestion, e.g. inhalation or transdermally. Salicylate and paracetamol are extremely common agents in self-poisoning and patients often present with no alteration of consciousness.

Investigation

All patients require urea and electrolyte, blood glucose and blood gas estimations. Rapid bedside kits detect the presence of common agents such as paracetacol, aspirin, and several recreational drugs. Urine samples and gastric aspirate should be saved for possible later toxicology analysis. Salicylate and paracetamol levels are necessary due to the common lack of early signs and to allow specific early treatment. Other drug levels may help in diagnosis but treatment is often supportive. Early support from the local Poisons Information Service should be solicited.

Supportive treatment

Treatment of cardiovascular and respiratory compromise and neurological disturbance is by standard methods outlined elsewhere in the book. In the unconscious patient, opiates and benzodiazepines may be reversed temporarily to allow assessment of underlying neurological status.

Gastric elimination

Consider gastric emptying if the poison is not a corrosive or hydrocarbon and has been ingested <4h previously. If salicylates or tricyclics have been ingested gastric emptying is useful for 12h after ingestion. There are no clear advantages for forced emesis (ipecacuanaha 30ml in 200ml water) or gastric lavage. Forced emesis may be delayed for 30min and then may be intractable. Aspiration is a serious risk with either form of gastric emptying therapy; the patient should be intubated for airway protection if consciousness is at all impaired.

Activated charcoal

Activated charcoal is probably more effective than gastric emptying to prevent drug absorption. A charcoal:poison weight ratio of 10:1 is required. Poisons may be eliminated after absorption via the small bowel with activated charcoal 50–100g followed by 12.5g/h NG. Activated charcoal is particularly useful for benzodiazepines, anticonvulsants, tricyclics, theophylline, phenothiazines and antihistamines.

Forced diuresis and dialysis

Forced diuresis with appropriate urinary acidification or alkalinisation (see table) is useful for water-soluble poisons which are distributed predominantly extracellularly. Forced diuresis should not be used if renal function is abnormal. Small molecules may also be removed by haemodialysis (e.g. ethylene glycol, methanol, oxalic acid, formic acid).

Forced alkaline diuresis

- Used for soluble acidic drugs (e.g. salicylates)

- Furosemide or mannitol to maintain urine output >200ml/h

- Intravenous crystalloid to prevent hypovolaemia

- Avoid excessive positive fluid balance

- Use 1.26% bicarbonate to maintain urinary pH >7

- Stop bicarbonate if arterial pH >7.5 and use 0.9% saline

- Alternate bicarbonate/saline with 5% glucose

- Monitor and replace potassium and magnesium carefully

Forced acid diuresis

- Used for soluble basic drugs (e.g. amphetamines, quinine, phencyclidine)

- Furosemide or mannitol to maintain urine output >200ml/h

- Intravenous crystalloid to prevent hypovolaemia

- Avoid excessive positive fluid balance

- Use 750g NH_4Cl in each 500ml 5% glucose to maintain urinary pH <7.0

- Alternate 0.9% saline with 5% glucose

- Monitor and replace potassium and magnesium carefully

See also:

Ventilatory support—indications, p4; Endotracheal intubation, p36; ECG monitoring, p108; Blood pressure monitoring, p110; Toxicology, p162; Respiratory stimulants, p188; Basic resuscitation, p270; Respiratory failure, p282; Hypotension, p312; Tachyarrhythmias, p316; Bradyarrhythmias, p318; Salicylate poisoning, p454; Paracetamol poisoning, p456; Sedative poisoning, p458; Tricyclic antidepressant poisoning, p460; Amphetamines including Ecstasy, p462; Cocaine, p464; Inhaled poisons, p466; Household chemicals, p468; Methanol and ethylene glycol, p470; Organophosphate poisoning, p472; Rhabdomyolysis, p528

Salicylate poisoning

Serious, life-threatening toxicity is likely after ingestion of >7.5g salicylate. Aspirin is the most common form ingested though salicylic acid and methylsalicylate are occasionally implicated.

Loss of consciousness is rare but metabolic derangements are complex (e.g. respiratory alkalosis due to respiratory centre stimulation, dehydration due to salt and water loss, renal bicarbonate excretion and hyperthermia, hypokalaemia, metabolic acidosis due to interference with carbohydrate, lipid and amino acid metabolism, hyperthermia due to uncoupling of oxidative phosphorylation and increased metabolic rate).

There may also be pulmonary oedema due to capillary leak, and bleeding due to reduced prothrombin levels.

Although gastric erosions are common with aspirin treatment, bleeding from this source is rare in acute poisoning.

Management

Gastric elimination

Due to delayed gastric emptying gastric elimination is worthwhile for up to 24h after ingestion. Activated charcoal (12.5g/h) should be given NG to adsorb salicylate remaining in the bowel and adsorb any salicylate back- diffusing across the bowel mucosa. Insoluble aspirin may form a gastric mass that is difficult to remove by gastric lavage.

Salicylate levels

Repeated levels should be taken since these may continue to rise as absorption continues. Levels taken after 12h may underestimate the degree of toxicity due to tissue binding. If salicylate levels are <3.1mmol/l after 1h of ingestion and there is no metabolic derangement then observation, fluids and repeat levels are all that is required. Urine alkalinization is required if levels are >3.1mmol/l or there is metabolic derangement but no renal failure. Levels >6.2mmol/l (or >3.1mmol/l with renal failure) require haemodialysis.

Alkaline diuresis

The alkalinisation rather than the forced diuresis is more important for salicylate excretion. Urinary pH must be >7.0

without arterial alkalosis (pH <7.5). Potassium loss will occur with the bicarbonate infusion, due to the diuresis and as a toxic effect of the salicylate. Potassium levels must be monitored and corrected in a high dependency environment. Alkalinization, if successful, should continue until salicylate levels <3.1mmol/l. Calcium levels may drop with prolonged alkalinization.

Haemodialysis
Indications include salicylate levels >6.2mmol/l or renal failure.

See also:
Blood gas analysis, p100; Toxicology, p162; Hypokalaemia, p422; Metabolic acidosis, p434; Poisoning—general principles, p452

Paracetamol poisoning
Serious, life-threatening toxicity is likely after ingestion of >15g paracetamol, particularly with co-ingestion of enzyme-inducing drugs (e.g. anticonvulsants, anti-TB therapy) and/or alcohol.

Paracetamol is rapidly absorbed from the stomach and upper small bowel and is metabolised by conjugation in the liver. Hepatic necrosis occurs due to the toxicity of an alkylating metabolite that is normally removed by conjugation with glutathione; glutathione is rapidly depleted with overdose and may already be low in starvation, alcoholics and, possibly, HIV disease, thus predisposing these groups to an increased risk of toxicity.

Toxicity is usually asymptomatic for 1–2 days although laboratory assessment of liver function may become abnormal after 18h.

Hepatic failure, if manifest, develops after 2–7 days, an earlier onset being associated with more severe toxicity.

Management
If ingestion has occurred <4h previously, gastric elimination techniques should be employed. Paracetamol levels may be taken to confirm ingestion but should not be interpreted for toxicity until after 4h from ingestion. The mainstay of treatment is with *N*-acetylcysteine to restore hepatic glutathione levels by increasing intracellular cysteine levels.

N-acetylcysteine
Treatment is most effective if started within 10h of ingestion but is currently advised for up to 36h of ingestion. Treatment is required if the paracetamol levels are in the toxic range (see figure) or >15g paracetamol has been ingested. It should be continued until paracetamol is not detected in the blood. *N*-acetylcysteine is given by continuous IV infusion (150mg/kg over 15min, 50mg/kg in 500ml 5% glucose over 4h then 50mg/kg in 500ml 5% glucose 8-hrly).

Complications
The major complication is hepatic (± renal) failure. A rise in prothrombin time, INR and bilirubin are early warning signs of significant hepatic damage and this should prompt early referral to a specialist centre.

Guidelines for referral to a specialist liver centre

- Arterial pH <7.3
- INR >3 on day 2 or >4 thereafter
- Oliguria and/or rising creatinine
- Altered conscious level
- Hypoglycaemia

Guidelines for liver transplantation

- Arterial pH <7.3

  Plus all of the following:

- PT >100, INR >6.5
- Creatinine >300µmol/l
- Grade 3–4 encephalopathy

  High lactate levels (>3.5mmol/l at 4 and 12h) and low factor V levels are also associated with a poor outcome if not transplanted.

Graph for predicting treatment requirement
Treatment is required at lower levels if the patient is a known alcoholic, protein-depleted, HIV positive, or is taking enzyme-inducing drugs, e.g. phenytoin.

Figure. No Caption Available.
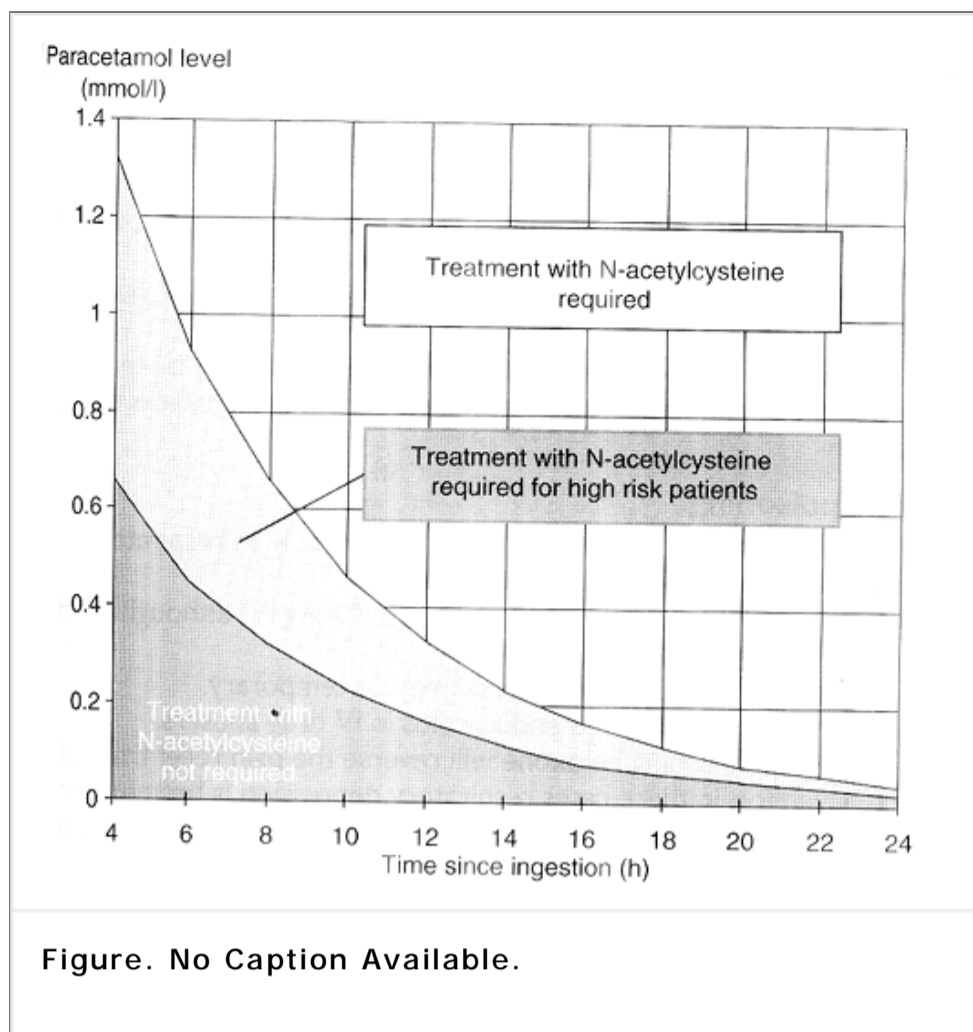
See also:

Liver function tests, p152; Coagulation monitoring, p156; Toxicology, p162; Acute renal failure—diagnosis, p332; Acute renal failure—management, p334; Acute liver failure, p360; Hepatic encephalopathy, p362; Poisoning—general principles, p452

Sedative poisoning

Patients present with alteration of consciousness, respiratory failure and, in some cases, cardiovascular disturbance. After prolonged immobility the possibility of rhabdomyolysis should be considered. In most cases treatment is supportive.

Benzodiazepine poisoning

- Benzodiazepines are common agents used for self-poisoning but severe features are uncommon, except at extremes of age.
- Flumazenil may be used as a specific antidote (0.2–1.0mg IV given in 0.1mg increments).
- Flumazenil is short acting so benzodiazepine reversal may be temporary.
- Rapid reversal of benzodiazepines may lead to anxiety attacks or seizures.

Opioid poisoning

- Treatment is supportive with attention particularly to respiratory depression and cardiovascular disturbance.
- Naloxone may be used as an antidote (0.2–0.4mg IV) although rapid reversal is not desired in abusers.
- Naloxone is short acting so reversal may be temporary.
- Consider HIV infection and endocarditis in IV drug abusers.
- In iatrogenic poisoning naloxone will reverse the pain relief that opioids were given for. In these cases respiratory depression is better reversed by the non-specific respiratory stimulant doxapram (1.0–1.5mg/kg over 30s IV followed by 1.5–4.0mg/min).

Barbiturates

Treatment is supportive with particular attention to respiratory and cardiovascular depression. Vasodilatation may be extreme requiring fluid support and, in some cases, inotropic support. Phenobarbital may be eliminated by forced alkaline diuresis.

See also:

Ventilatory support—indications, p4; Blood gas analysis, p100; Blood pressure monitoring, p110; Toxicology, p162;

Tricyclic antidepressant poisoning

Tricyclic antidepressants are prescribed to patients who are at greatest risk of a suicide attempt. They are rapidly absorbed from the gastrointestinal tract, although gastric emptying is delayed.

Clinical features

- Anticholinergic effects (dilated pupils, dry mouth, ileus, retention of urine).

- Arrhythmias (particularly associated with prolonged QT interval and QRS waves).

- Hypotension related to arrhythmias and/or cardiac depression through Na^+ channel blockade.

- Hyper-reflexia with extensor plantars, visual hallucinations, coma and seizures. Drug levels do not correlate with severity.

- Metabolism is usually rapid and improvement can be expected within 24h.

Management

1. There is no specific treatment for tricyclic antidepressant poisoning.

2. Patients require ECG monitoring during the first 24h and until ECG changes have disappeared for 12h.

3. Gastric elimination is worthwhile for 24h after ingestion since tricyclics slow gastric emptying.

4. Activated charcoal via a nasogastric tube will adsorb tricyclics remaining in the bowel.

5. Cardiac arrhythmias are more common if there is acidosis. Bicarbonate should be used to achieve an arterial pH of 7.5 urgently. If arrhythmias occur with no acidosis and fail to respond to treatment with amiodarone or phenytoin, bicarbonate (25–50ml 8.4% IV) may still be useful.

6. Seizures are best managed with benzodiazepines and phenytoin.

See also:

Amphetamines including Ecstasy

Amphetamines, including 3,4-methylenedioxymethamphetamine (MDMA, 'Ecstasy') and 3,4-methylenedioxyethamphetamine ('Eve'), are stimulants taken predominantly for recreational use, or as appetite suppressants. These drugs are hallucinogenic at higher doses. MDMA has been shown to cause rapid decreases in central nervous system 5-hydroxytryptamine and 5-hydroxyindole-3-acetic acid levels and increases in dopamine release.

Clinical features of overdose

Agitation, hyperactivity, hypertension, hallucinations, paranoia followed by exhaustion, coma, convulsions and hyperthermia.

Idiosyncratic responses to Ecstasy and Eve are more common, with numerous reports of mortality and major morbidity following ingestion of just 1–2 tablets. These appear related to ingestion in hot environments, e.g. nightclubs, and concurrent dehydration. Features include profound hyperthermia (>40°C), agitation, seizures, muscle rigidity, hypertension, tachycardia, sweating, coma, disseminated intravascular coagulation and rhabdomyolysis. These complications lead to hypovolaemia, electrolyte imbalance (particularly hyperkalaemia) and a metabolic acidosis.

Some patients taking Ecstasy or Eve have been admitted with water intoxication and acute hyponatraemia following ingestion of large amounts of water.

Management

1. Supportive care including airway protection, fluid resuscitation, electrolyte correction and, if needed, mechanical ventilation.

2. Early stages of amphetamine poisoning can often be controlled with tepid sponging, chlorpromazine, β-blockade. Forced acid diuresis to increase urinary excretion is rarely needed.

3. Severe complications should be managed as they arise, e.g. rapid cooling for hyperpyrexia, anticonvulsants for seizures, forced alkaline diuresis ± fasciotomies for rhabdomyolysis, platelet and fresh frozen plasma infusions for coagulopathy.

4. Dantrolene may be given to treat the hyperpyrexia at a dose of 1mg/kg IV, repeated to a cumulative maximum dose of 10mg/kg, particularly if the temperature is >40°C.

See also:

Ventilatory support—indications, p4; Blood gas analysis, p100; ECG monitoring, p108; Blood pressure monitoring, p110; Toxicology, p162; Basic resuscitation, p270; Hypertension, p314; Tachyarrhythmias, p316; Generalised seizures, p372; Poisoning—general principles, p452; Hyperthermia, p522

Cocaine poisoning

Modes of action

- Blocks reuptake of dopamine (causing euphoria, hyperactivity) and noradrenaline (causing vasoconstriction and hypertension)
- Blocks Na^+ channels, resulting in a local anaesthetic action and myocardial depression
- Platelet activation

Complications

- Chest pain related to myocardial ischaemia or infarction. Local chest pain guidelines should be followed. ECG abnormalities often resolve within 12h. Arrhythmias should be treated conventionally, though avoiding β-blockers.
- Heart failure from myocardial depression or a cardiomyopathy
- Seizures
- Cerebrovascular accidents
- Pneumothorax
- Rhabdomyolysis
- Premature labour—abruption
- Agitated delirium, hyperthermia
- Thermal injury from smoke inhalation

Management

1. Oxygen
2. Diazepam for agitation, delirium, chest pain
3. Aspirin for chest pain, CVA
4. Nitrates for chest pain, heart failure
5. Sodium bicarbonate and forced diuresis for rhabdomyolysis
6. β-blockers should be avoided

See also:

Oxygen therapy, p2; Ventilatory support—indications, p4; Blood gas analysis, p100; ECG monitoring, p108; Blood pressure monitoring, p110; Toxicology, p162; Basic resuscitation, p270; Hypertension, p314; Tachyarrhythmias, p316; Acute coronary syndrome (1), p320; Acute coronary syndrome (2), p322; Generalised seizures, p372; Stroke, p380; Poisoning—general principles, p452; Hyperthermia, p522; Rhabdomyolysis, p528

Inhaled poisons

Carbon monoxide

Carbon monoxide poisoning should be considered in anyone found in a smoke filled, enclosed space. Carbon monoxide displaces oxygen from haemoglobin, to which it has 200 times greater affinity and thus prevents oxygen carriage. There is also a direct toxic effect on mitochondrial oxidative phosphorylation as it competes with oxygen for the same binding site on cytochrome oxidase.

Clinical features

- Fatigue, headache, vomiting, dizziness, confusion, dyspnoea.

- A cherry red appearance of the skin and mucosae are classical but not common.
- PaO_2 will be normal unless there is respiratory depression and pulse oximetry is misleading.
- The half life of carboxyhaemoglobin is 4h when breathing room air and 50min when breathing 100% oxygen.

Management

- Carboxyhaemoglobin levels should be measured by a co-oximeter and treatment started immediately with oxygen at the maximum concentration that can be delivered (FIO_2 1.0 if ventilated and 0.6–1.0 if self-ventilating).
- If carboxyhaemoglobin levels >25% or carbon monoxide poisoning is associated with mental disturbance, the optimal treatment is hyperbaric oxygen at 3 atmospheres for 30min, repeated 6-hrly if levels remain >25%. Death is likely with carboxyhaemoglobin levels >60%.
- High concentration oxygen treatment should continue until carboxyhaemoglobin levels <10%.

Cyanide

- Severe cyanide poisoning has an extremely rapid onset and occurs in some cases of smoke inhalation. Survival may be associated with anoxic brain damage.
- Diagnosis must be made clinically since a blood cyanide level takes >3h to perform.

Clinical features
Clinical features include anxiety, agitation, hyperventilation, headache, loss of consciousness, dyspnoea, weakness, dizziness and vomiting. The skin remains pink and hypotension may be severe. An unexplained metabolic acidosis is suggestive.

Management

- High concentration oxygen should be given, but is only truly effective when given at hyperbaric pressures.
- In mild cases rapid, natural detoxification reduces cyanide levels by 50% within 1h, allowing supportive therapy only.
- Sodium thiosulphate (150mg/kg intravenously followed by 30–60mg/kg/h) converts cyanide to thiocyanate and should be used if there is unconsciousness. It is, however, slow-acting.
- Nitrites produce methaemoglobinaemia and may potentially worsen cyanide toxicity.
- Dicobalt edetate (300mg IV) is the specific antidote to cyanide but is severely toxic (vomiting, urticaria, tachycardia, hypotension, dyspnoea, chest pain) in the absence of cyanide. It is therefore best avoided unless cyanide toxicity is likely.

Key trial
Weaver LK, et al. Hyperbaric oxygen for acute carbon monoxide poisoning. N Engl J Med 2002; 347:1057–67

See also:
Oxygen therapy, p2; Ventilatory support—indications, p4; Blood gas analysis, p100; ECG monitoring, p108; Blood pressure monitoring, p110; Toxicology, p162; Basic resuscitation, p270; Inhalation injury, p306; Metabolic acidosis, p434; Poisoning—general principles

Household chemicals

Corrosives
Strong acids and alkalis are increasingly available in the household and ingestion may lead to shock and bowel perforation. Gastric elimination techniques must be avoided since aspiration of corrosives may cause severe lung damage. Early surgical repair of perforation may be necessary.

Petroleum
Although not strictly a household chemical, access to petroleum in the home is easy.

Clinical features
Gastrointestinal ingestion and absorption gives clinical features similar to those of alcohol intoxication with more severe central nervous system depression.

Management

- Gastric elimination techniques must be avoided since a few drops of petroleum spilling into the lungs can lead to a severe pneumonitis. This is due to the low surface tension and vapour pressure of petroleum allowing rapid spread through the lungs.
- Treatment involves supportive therapy and 250ml liquid paraffin orally.

Paraquat

Paraquat is widely available as a selective weedkiller which is inactivated on contact with the soil. A dose of 2–3g is usually fatal (equivalent to 80–120g of granules or 10–15ml of industrial liquid concentrate).

Clinical features

- Very little of the ingested paraquat is absorbed from the gut but a large dose will lead rapidly to shock with widespread tissue necrosis.
- A burning sensation in the mouth and abdomen is more common in poisoning, as is the development of painful mouth ulcers and, after several days, a relentless, proliferative alveolitis causing death by pulmonary fibrosis.

Management

- Treatment should begin on clinical grounds in view of the severity of toxicity and the time taken for laboratory confirmation.
- Urgent gastric emptying is required with instillation of 500ml water containing 150g Fuller's earth and 25g magnesium sulphate afterwards.
- Severe diarrhoea may ensue requiring careful fluid management.
- If paraquat poisoning is confirmed 200–500ml of 30% Fuller's earth is given 2-hrly for 24h via a nasogastric tube.
- A forced diuresis should be started to encourage renal excretion.
- Pulmonary fibrosis is more severe when breathing high oxygen concentrations; if oxygen is required the lowest concentration possible should be given accepting a low PaO_2. Liposomal superoxide dismutase and glutathione peroxidase have been used experimentally.

See also:

Methanol and ethylene glycol

Methanol

Toxicity mainly arises due to oxidation of methanol to formic acid and formaldehyde. The oxidative pathway is an enzymatic process involving alcohol dehydrogenase but proceeds at 20% of the rate of ethanol oxidation.

Clinical features

Clinical features of poisoning include blindness (due to concentration of methanol in the vitreous humour), severe metabolic acidosis, headache, nausea, vomiting and abdominal pain.

Management

- Metabolism of methanol is slow so treatment will need to be prolonged (several days).
- Treatment includes gastric emptying (within 4h of ingestion), sodium bicarbonate titrated to correct arterial pH and ethanol to saturate the oxidative pathway.
- On presentation 1ml/kg ethanol (50%) is given orally followed by 0.5ml/kg 2-hrly for 5 days.
- Alternatively, metabolism can be blocked by 4-methyl pyrazole (fomepizole) which can be infused or injected 12-hrly.
- If methanol levels are >1000mg/l haemodialysis is used until levels are <250mg/l.

Ethylene glycol

Ethylene glycol is partially metabolised by alcohol dehydrogenase to oxalic acid which is responsible for a severe metabolic acidosis, renal failure and seizures.

Clinical features

Clinical suspicion is aroused by odourless drunkenness, oxalate crystals in the urine or blood and the severe acidosis. As little as 50ml can be fatal.

Management

Treatment is as for methanol.

See also:

Organophosphate poisoning

Organophosphate pesticides are the major cause of suicidal poisoning in developing countries and are used as nerve agents in terrorist attacks (e.g. Sarin, Tabun, VX, GF). Their mode of action is via cholinergic toxicity.

Cholinergic (anticholinesterase) syndrome

- Salivation, lacrimation
- Vomiting, diarrhoea
- Bradycardia
- Bronchospasm
- Meiosis

Management

- Atropine—antagonises acetylcholine at muscarinic receptors. A dose of 2mg should be given every 15min until the mouth is dry
- Pralidoxime—reactivates inhibited enzymes if given before the agent permanently binds to the enzyme
- Diazepam—neuroprotection

See also:

Ovid: Oxford Handbook of Critical Care

Infection and Inflammation

Infection control—general principles

Infection acquired within the ICU is a major cause of mortality, morbidity and increased duration of stay. There are remarkable variations in practice for which the lack of a good evidence base is chiefly responsible. Examples include different policies with regard to patient isolation, microbiological surveillance, handwashing procedures, use of impregnated vascular catheters, the duration of indwelling catheters, and frequency of change of disposables such as intravenous giving sets and filters. It is nevertheless accepted that adequate handwashing before and after patient contact and strict aseptic technique when performing procedures are mandatory.

ICU design

- Ample wash hand basins with elbow operated mixer taps, soap and antiseptic dispensers
- Separate clean-treatment and sluice areas
- Some isolation cubicles with positive/exhaust air flow facility
- Ample space around bed areas

Staff measures

- Remove watches and jewellery, remove long-sleeve white coats and jackets, roll shirt sleeves up to elbow

- Hand and forearm washing before and after touching patient

- Wear disposable aprons and gloves if in contact with patient

- Wear gloves and aprons when handling any body fluid and eyeprotection when any danger of fluid or droplet splash

- Strict aseptic technique for invasive procedures (e.g. central venous catheter insertion) and clean technique for basic procedures, e.g. endotracheal suction, changing ventilator circuits or drug infusions

- Previous immunisation against hepatitis B, tuberculosis

- Stethoscopes should be cleaned between patients

- Clear sign-posting of precautions to be taken on cubicle doors

Visitors

- Non-ICU medical and paramedical staff, relatives and friends should adhere to the guidelines in force regarding the patient being visited, e.g. hand washing, gowns and gloves as directed.

- Traffic through the ICU should be minimised.

Cross-infection

- Inform the Infection Control nurse should cross-infection arise with more than one patient infected by the same strain of bacteria.

- Affected patients should generally be source isolated, especially if the organism is multiresistant; treated with antibiotics and topical antiseptics if necessary; and barrier-nursed.

- If cross-infection persists/spreads, other sources should be sought, e.g. taps, sinks, reusable equipment (rebreathing bags, ventilators).

Protective isolation

- Some patients carry potentially contagious or infective organisms and require source isolation, e.g. tuberculosis.

- Immunosuppressed patients, e.g. when neutropenic following chemotherapy, are at risk of acquiring infection.

Microbiological surveillance

Policies vary; some ICUs routinely screen sputum, bronchoalveolar lavage, blood, urine and drain fluid every 3–7 days while others screen only when indicated, e.g. deteriorating cardiorespiratory status, pyrexia, neutrophilia. Send samples promptly to the lab for analysis.

See also:

Bacteriology, p158; Virology, serology and assays, p160; Antimicrobials, p260; Acute chest infection (1), p288; Acute chest infection (2), p290; Infection—diagnosis, p480; Infection—treatment, p482; ICU layout, p566

Routine changes of disposables

Care of intravascular catheters

- Sites should be covered with transparent semipermeable dressings to allow observation and prevent secretions from accumulating.

- Routine changes of intravascular catheters are no longer recommended. As the risk of infection does increase considerably after a week *in situ*, catheters should be removed as soon as clinically feasible.

- Catheters can be changed over a guidewire if the site looks clean but signs suggestive of mild to moderate infection are present elsewhere, (e.g. pyrexia or unexplained neutrophilia) but without major cardiorespiratory disturbance.

- Catheters should be changed to a fresh site if:
  - the old site appears infected
  - the patient shows signs of severe infection
  - a positive growth is obtained from a blood culture drawn through the catheter or from the tip of the previous catheter

Routine changes of disposables

	Frequency
Ventilator circuit (if using bacterial filters)	Between patients unless soiled
Ventilator circuit (if using water bath humidifier)	Daily
Endotracheal tube catheter mount and bacterial filter	Between patients unless soiled
Disposable oxygen masks	Between patients unless soiled
CPAP circuits	Between patients unless soiled
Rebreathing bags and masks	Between patients unless soiled
Intravenous infusion giving sets	48h
Parenteral nutrition giving sets	Daily
Enteral feeding giving sets	Daily
Arterial/venous pressure transducer sets	48h
Wound dressings	Depends on type of dressing
Tracheostomy site	As necessary
Urinary catheter bags	Weekly

Infection—diagnosis

Infection is both a common cause of admission to intensive care and the major secondary complication. Critically ill patients are predisposed to further nosocomial infections as many of their natural barriers and defence mechanisms have been lost, altered or penetrated. They are often heavily instrumented, sedated and immobile. They often develop immune hyporesponsiveness as part of their critical disease process, notwithstanding any therapeutic immune suppression they may have received. The high antibiotic load given to these sick patients encourages colonisation by pathogenic organisms and subsequent development of infections by multidrug resistant and/or atypical (e.g. fungi) organisms.

Sepsis is defined as the systemic response to an insult of proven or high likelihood of infection. Whereas infection can be applied to a localised phenomenon, sepsis initiates a systemic inflammatory response thereby affecting distant organs.

Diagnosis

- Often problematic in the critically ill patient as focal signs may be lacking and/or camouflaged by concurrent disease (e.g. ventilator-associated pneumonia on top of ARDS). Symptoms are often notforthcoming due to the patient's mentally incompetent state.

- In addition, all of the traditional clinical and biochemical markers of infection are non-specific. These include pyrexia, neutrophilia and altered sputum. Furthermore, the frequent presence of colonising organisms e.g. MRSA on skin, *Pseudomonas aeruginosa* in the respiratory tract, does not imply concomitant infection. As a consequence, many patients are over-treated with antibiotics, enhancing the risk ofovergrowth of resistant/atypical organisms.

- Markers of inflammation (C-reactive protein, procalcitonin) may be useful, though studies have produced conflicting results as to their specificity/sensitivity in diagnosing underlying infection.

- The value of routine screening (microbiological surveillance) is not proven, though this may help to identify infecting organisms earlier.

- For cases of suspected infection, appropriate samples should be taken for analysis including blood, sputum, wound swabs, drainage fluid, aspirated pus, catheter tips, cerebrospinal fluid, etc. These shouldgenerally be taken before new antibiotics are commenced.

- Consider less common causes of infection such as endocarditis or osteomyelitis, particularly if the patient fails to settle after a standard course of therapy.

Differential diagnosis of pyrexia

- Infection
- Non-infective causes of inflammation, e.g. trauma, surgery, burns, myocardial infarction, vasculitis, hepatitis, acalculous cholecystitis, pancreatitis
- Adverse drug reactions
- Excessive ambient heating
- Miscellaneous causes, e.g. neoplasm

Definitions

Infection
Microbial phenomenon characterised by an inflammatory response to the presence of micro-organisms or the invasion of normally sterile host tissue by those organisms

Bacteraemia
The presence of viable bacteria in the blood.

Sepsis
The systemic response to infection. Definition as for SIRS but as a result of infection.

Sites of infection before and after admission to an ICU

Organ	Primary site of infection needing admission to ICU	Secondary site of infection acquired while in ICU
Brain	+	+
Sinuses	-	+
Cannula/wound sites	+ +	+ + + + +
Other skin and soft tissue	+ +	+
Chest	+ + + +	+ + + +
Urogenital tract	+ +	+
Abdomen	+ + + +	+ +
Bone	+	+
Heart valves	+	+

Key paper
American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med 1992; 20:864–74.

See also:

Infection—treatment

Treatment

- Drain pus
- Change cannula sites if necessary

- Appropriate antibiotic therapy after laboratory specimens taken—though this may not be necessary for mild infections where the cause has been removed, e.g. an infected catheter

- Radiological and/or surgical intervention if indicated

Regular input from microbiological ± infectious disease specialists isrecommended to advise on best options for empiric therapy and for possible modifications based on early communication of laboratory results (including antibiotic sensitivity patterns).

Empiric antibiotic therapy is guided on the severity of illness of the patient, likely site of infection and likely infecting organism(s), whether the infection is community-acquired or nosocomial (including ICU-acquired), patient immunosuppression, and known antibiotic resistance patterns of hospital and local community organisms. In general, critically ill patients should receive parenteral antibiotics at appropriate dosage, taking into account any impaired hepatic or renal clearance, or concurrent renal replacement therapy. Broad-spectrum therapy may be initially needed, with refinement, cessation or change after 2–3 days depending on clinical response and organisms subsequently isolated. The duration of treatment remains highly contentious. Apart from specific conditions such as endocarditis, tuberculosis and meningitis, where prolonged therapy is probably advisable, it may be sufficient to stop within 3–5 days provided the patient has shown adequate signs of recovery. Alternatively, patients not responding or deteriorating should be considered to be either treatment failures or inappropriately treated (i.e. no infection was present in the first place).As described earlier, commonly accepted markers of infection are poorly specific in the intensive care patient. Indeed, pyrexia may settle on stopping antibiotic treatment. Cessation or change of antibiotic therapy must be considered on individual merits according to the patient's condition and any subsequent laboratory results. An advantage of ceasing therapy is the ability to take further specimens for culture in an antibiotic-free environment.

It may be necessary to remove indwelling pacemakers, tunnelled vascular catheters, prosthetic joints, plates, implants, grafts and stents if these are the suspected cause of infection. This should be done in consultation with microbiologists and the appropriate specialist as individual risk and benefit needs to be carefully weighed up.

Specimen antibiotic regimens (organism unknown)

Sepsis of unknown origin	2nd/3rd generation cephalosporin OR quinolone OR carbapenem OR piptazobactam
	± aminoglycoside (if Gram negative suspected)
	± metronidazole (anaerobic cover)
	± glycopeptide or linezolid (if MRSA suspected)
Pneumonia—community acquired	2nd/3rd generation cephalosporin + macrolide
Pneumonia—nosocomial	3rd generation cephalosporin OR quinolone OR carbapenem OR piptazobactam ± aminoglycoside (if Gram negative suspected)
	+ teicoplanin, vancomycin
	+ rifampicin or linezolid (if MRSA likely)
Skin and soft tissue	Flucloxacillin (if MSSA likely)
	Glycopeptide or linezolid (if MRSA likely)
	Benzyl penicillin or clindamycin (if *Streptococcus* suspected)
Abdominal	2nd/3rd generation cephalosporin OR quinolone OR carbapenem OR piptazobactam
	± aminoglycoside
	± metronidazole
Gynaecological	2nd/3rd generation cephalosporin OR quinolone OR carbapenem OR piptazobactam
	± aminoglycoside
	+ metronidazole
Nephrourological	2nd/3rd generation cephalosporin OR quinolone OR carbapenem OR piptazobactam
	± aminoglycoside

See also:

Blood pressure monitoring, p110; Bacteriology, p158; Antimicrobials, p260; Acute chest infection (1), p288; Acute chest infection (2), p290; Hypotension, p312; Abdominal sepsis, p350; Meningitis, p374; Tetanus, p390; Botulism, p392; Neutropenia, p408; Systemic inflammation/multi-organ failure, p484; Sepsis and septic shock—treatment, p486; HIV related disease, p488; Malaria, p490; Pyrexia (1), p518; Pyrexia (2), p520; Post-operative intensive care, p534

Systemic inflammation/multi-organ failure

Exposure to an exogenous insult can result in an exaggerated, generalised and often inappropriate inflammatory response. This is described as 'SIRS'—the systemic inflammatory response syndrome. Stimulation of inflammatory pathways leads to activation of macrophages, endothelium, neutrophils, platelets, coagulation, fibrinolytic and contact systems with release of inflammatory mediators and effectors (e.g. cytokines, prostanoids, free oxygen radicals, proteases, nitric oxide, endothelin). This results in microvascular obstruction and occlusion, blood flow redistribution, interstitial oedema and fibrosis, and cellular mitochondrial dysfunction. The consequences of this may be organ dysfunction, varying from 'mild' to severe, and affecting single or multiple organs, resulting in cardiovascular collapse, gastrointestinal failure, renal failure, hepatic failure, encephalopathy, neuropathy,

myopathy, and/or disseminated intravascular coagulation. Acute respiratory distress syndrome (ARDS) is the respiratory component of this pathophysiological response.

Causes include:

- Infection
- Trauma, burns
- Pancreatitis
- Inhalation injuries
- Massive blood loss/transfusion
- Miscellaneous including drug-related (including overdose), myocardial infarction, drowning, hyperthermia, pulmonary embolus

Treatment

Largely supportive, though the cause should be removed/treated if at all possible. Treatment includes antibiotics, drainage of pus, fixation of femoral/ pelvic fractures and debridement of necrotic tissue.

An important facet of organ support is to minimise iatrogenic trauma. It is sufficient to maintain survival with relative homeostasis until recovery takes place rather than attempting to achieve normal physiological or biochemical target values. An example of this is permissive hypercapnia.

Specific treatment regimens remain contentious due to a lack of adequately powered studies showing optimal haemodynamic goals, inotropic/ pressor agents, antibiotic regimens, etc. Local policies may favour the use of one or more of a range of eclectic therapies that may offer a reasonable theoretical basis for administration, or anecdotal success, though theseall remain essentially unproven. Examples include antioxidants, protease inhibitors, immunonutrition, plasmapheresis, vasodilators, and immunoglobulins. It is generally agreed that rapid resucitation and restoration of oxygen delivery, glycaemic control and prompt removal of any treatable cause is desirable in preventing the onset of SIRS.

Because of non-standardisation of definitions, outcome data are conflicting, though single organ 'failure' carries an approximate 20–30% mortality while ≥3 organ 'failures' lasting ≥3 days carries a mortality in excess of 50%. Recovery is often complete in survivors, though recent studies are revealing long term physical and psychological sequelae in a significant proportion of patients.

Current UCL Hospitals principles of management

Respiratory	$SaO_2 > 90$–95% (may have to settle for lower) Permissive hypercapnia
Cardiovascular	Maintain cardiac output/oxygen delivery and blood pressure compatible with adequate organ perfusion (e.g. no metabolic acidosis)
Renal	Maintain adequate metabolic and fluid homeostasis by intravascular filling, diuretics, vasoactive agents, and/or haemo(dia)filtration
Haematological	Maintain haemoglobin >7g/dl (unless cardiorespiratory problems), platelets >20–40 × 10^9/l, INR <1.5–2.5
Gastrointestinal	Stress ulcer prophylaxis (generally by enteral nutrition), pancreatitis, acalculous cholecystitis
Infection	Antibiotics, pus drainage, good infection control
Nutrition	Preferably early and by enteral route
Pressure area/mouth/joint care	Frequent turns, low pressure support surfaces, nursing care and physiotherapy
Psychological	Support to both patient and family

Definitions

Systemic inflammatory response syndrome (SIRS)

Two or more of:

- Temperature >38°C or <36°C

- Heart rate >90bpm

- Respiratory rate > 20 breaths/min or $PaCO_2$ <32mmHg (4.3kPa)

- WBC >12,000 cells/mm^3, <4000/mm^3, or >10% immature forms

Sepsis
The systemic response to infection. Definition as for SIRS but as a result of infection.

Severe sepsis
Sepsis associated with organ dysfunction, hypoperfusion or hypotension. These may include, but are not limited to, lactic acidosis, oliguria or an acute alteration in mental status.

Septic shock
Sepsis with hypotension, despite adequate fluid resuscitation, plus presence of perfusion abnormalities.

Multi-organ dysfunction syndrome (MODS)
Presence of altered organ function in an acutely ill patient such that homeostasis cannot be maintained without intervention. Multiple organ failure (MOF) has not achieved worldwide uniformity of definition.

See also:
Ventilatory support—indications, p4; Blood pressure monitoring, p110; Bacteriology, p158; Antimicrobials, p260; Acute respiratory distress syndrome (1), p292; Acute respiratory distress syndrome (2), p294; Inhalation injury, p306; Hypotension, p312; Abdominal sepsis, p350; Pancreatitis, p354; Infection control—general principles, p476; Sepsis and septic shock—treatment, p486; Multiple trauma (1), p500; Multiple trauma (2), p502; Burns—fluid management, p510; Burns—general management, p512; Pyrexia (1), p518; Pyrexia (2), p520

Sepsis and septic shock—treatment

Principles of treatment
As for other causes of MODS, outcome in sepsis improves with:

1. Prompt diagnosis and treatment of the underlying cause

2. Rapid resuscitation to prevent prolonged tissue hypoxia

3. Good glycaemic control

4. Strict infection control

5. Recognition and appropriate treatment of secondary infections

6. Adequate nutrition

7. Recognition that 'normal' physiological/biochemical levels do not necessarily need to be attained while the patient is critically ill, provided he/she is not compromised: e.g. a mean BP of 55–60mmHg is often acceptable unless evidence of poor perfusion or ischaemia suggests higher levels should be sought

8. Avoidance of preventable mishaps, e.g. prolonged hypotension, pressure sores, thromboembolism

9. Temperature control in the range 36–38.5°C.

10. Prevention of contractures, early mobilisation, etc.

11. Specific treatments (see below)

Specific treatments for severe sepsis/septic shock

1. Activated protein C significantly improves outcome in patients with ≥2 organ dysfunctions if commenced within 48h of onset of severe sepsis. The PROWESS study mainly included patients presenting from the community and had numerous exclusion criteria, particularly related to those at increased risk of bleeding. Subsequent studies revealed <15% of septic patients presenting to ICUs meet both inclusion and exclusion criteria.

2. 'Low-dose' hydrocortisone (50mg qds) given for 7 days improved outcomes if commenced within 8h of septic shock presentation, though only in the subset with an abnormal cortisol response to synthetic ACTH. Our current practice is to start hydrocortisone after performing a Synacthen test and to discontinue this therapy if the test is normal.

3. For norepinephrine (NEPI)-resistant septic shock, i.e. high-output severe hypotension not responding to adequate fluid loading and a NEPI dose >0.4μg/kg/min, we consider careful administration of terlipressin or methylthioninium chloride. Until more data are forthcoming, these agents should be viewed as rescue therapies rather than a straight alternative for NEPI.

4. We occasionally use plasmapheresis, prostaglandins or high-output haemofiltration for resistant cases of septic

shock, particularly those with low cardiac outputs. We readily acknowledge the evidence base for these therapies is slight and our use is based on anecdotal success.
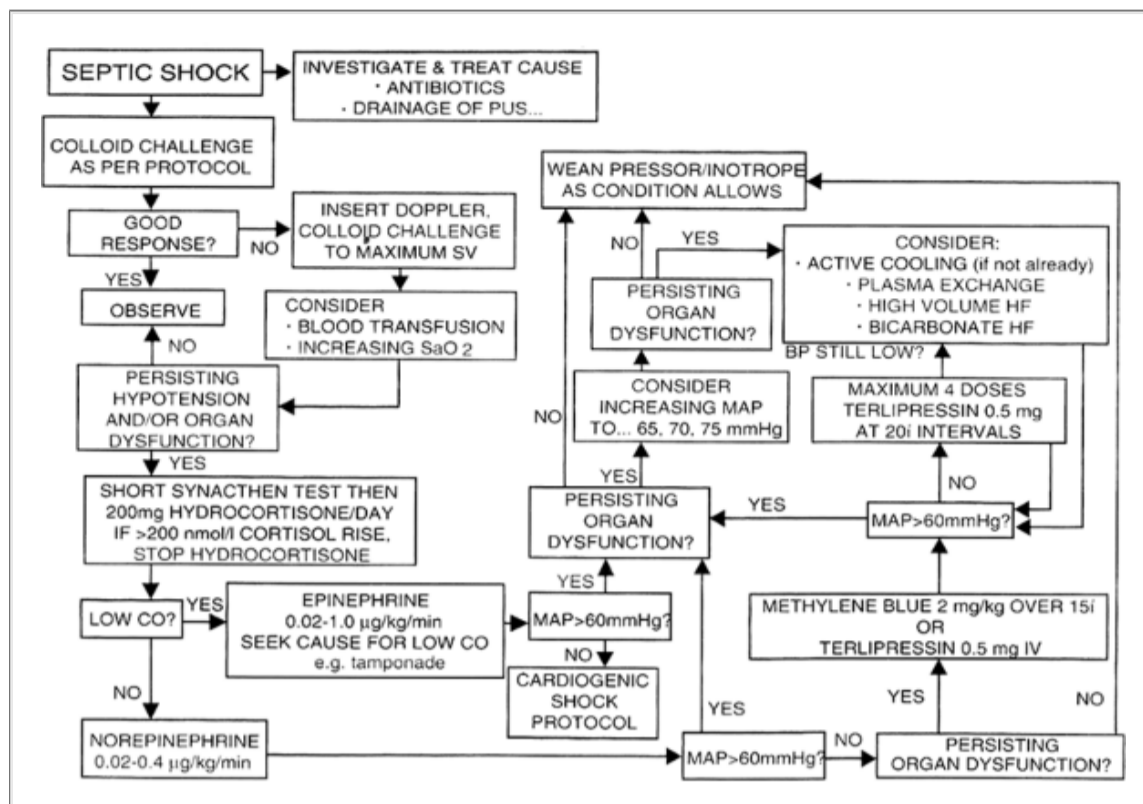
Figure. No Caption Available.

Key paper

Dellinger RP et al. Surviving Sepsis Campaign guidelines. Crit Care Med 2004; 32:858–73

Key trials

Bernard GR, for the PROWESS study group. Efficacy and safety of recombinant human activated protein C for severe sepsis. N Engl J Med; 344:699–709

Annane D, et al. Effect of treatment with low doses of hydrocortisone and fludrocortisone on mortality in patients with septic shock. JAMA 2002; 288:862–71

See also:

HIV related disease

Affected patients may present electively after diagnostic biopsies of brain or lung, or where elective ventilation is needed postoperatively. Other cases present with complications of HIV related disease, especially pulmonary infection (e.g. *Pneumocystis carinii*, CMV) or seizures (e.g. cerebral lymphoma, cerebral abscess, meningitis). HIV related diseases are now considered to be chronic manageable conditions with an often good short term prognosis. It is therefore reasonable that intensive care should be offered.

Infection control

The protection of staff from transmission of HIV follows basic measures. Body fluids should not be handled (wear gloves) and the face and eyes should be protected where there is a risk of splash contamination.

Needles should be disposed of in appropriate bins without re-sheathing. Any fluid spillages should be cleaned up immediately. Robust procedures are adhered to where a patient is known HIV positive; the real risk is in the patient of unknown HIV status. Remember that patients presenting with non-HIV related illness may be unknown positives. It follows that precautions should be taken for all patients.

Pneumocystis carinii pneumonia

- This is the commonest respiratory disorder affecting HIV positive patients. The majority survive their first attack but prognosis is not as good in those requiring mechanical ventilation. Intensive, early support with CPAP and appropriate chemotherapy may avert the need for ventilatory support.

- Treatment is usually started without waiting for laboratory confirmation.

- First line treatment is with high-dose co-trimoxazole or pentamidine with adjuvant high-dose steroids. Co-trimoxazole has a faster onset of effect and a broader spectrum of antibacterial activity covering the common secondary pathogens. Pentamidine is usually used where co-trimoxazole fails or where patients cannot take co-trimoxazole.

- Methylprednisolone is used to suppress peribronchial fibrosis andalveolar infiltrate. It is usual for there to be an initial deterioration on treatment lasting several days.

- Respiratory support is provided with CPAP (5–10cmH$_2$O) if hypoxaemic despite high FIO$_2$. Lower CPAP pressures should be used where possible as these patients are at risk of pneumothorax.

- Mechanical ventilation is reserved for those who have a rising with deteriorating gas exchange and fatigue despite CPAP.

- CXR changes respond very slowly.

Lactic acidosis

Nucleoside reverse transcriptase inhibitors (NRTIs) are frequently used anti-retroviral agents. However, an associated mitochondrial impairment can cause a severe lactic acidosis and a high mortality. Anecdotal use of L-carnitine is reported to be of benefit.

IV drug abusers

IV drug abusers are at high risk for HIV related disease, though present more commonly for other reasons (e.g. drug withdrawal syndromes, overdose, sepsis, endocarditis, hepatitis B or C, rhabdomyolysis).

Drug dosages

Co-trimoxazole	120mg/kg/day in divided doses IV for 10–14 days then PO to complete 21 days
Pentamidine	4mg/kg/day IV
Methylprednisolone	1g/day for 3 days

See also:

Malaria

Malaria should be suspected in any patient returning from endemic areas with a febrile illness which may have cerebral, abdominal, lung or renal features. Rarely, people living near airports may be bitten by a transported *Anopheles* mosquito. There may be considerable delay (weeks to months) between the mosquito bite and signs of infection. It is caused by protozoal infection with the *Plasmodium* genus. The most severe form is *P. falciparum* which causes malignant, tertian malaria. Other forms (*P. malariae*, *P. vivax*, *P. ovale*) rarely cause significant life threatening disease and will not be discussed further.

Pathophysiology

P. falciparum invades erythrocytes regardless of age. High levels of parasitaemia >5% are considered severe in non-immune travellers. The cells may haemolyse or be destroyed in liver or spleen. Anaemia may be severe. Increased vascular permeability, cytokine release, red cell agglutination and intravascular coagulation (DIC) may also occur.

Clinical features

- Symptoms include headache, fever with rigors, myalgia, abdominal pain, vomiting and diarrhoea. Signs include splenomegaly, jaundice, tender hepatomegaly and anaemia. Hyponatraemia is common.

- Only a minority of patients with *P. falciparum*have paroxysms of fever with 'cold' and 'hot' stages.

If >5% parasitaemia, features include:

- Cerebral malaria, causing coma, delirium, seizures or focal deficits.
- Cough and haemoptysis or acute respiratory distress
- Blackwater fever is associated with massive intravascular haemolysis, jaundice, haemoglobinuria, collapse and renal failure
- Acute renal dysfunction occurs in a third of adult ICU patients
- Acute cardiovascular collapse ('algid malaria') and metabolic acidosis
- Thrombocytopenia, DIC and spontaneous bleeding

Diagnosis

- Plasmodia seen in RBC in thick or thin smears of peripheral blood. The parasitaemia intensity may vary from hour to hour and may be scanty in number. The smear should be carefully scrutinised and repeated if doubt persists.
- Leucocytosis is not a feature of malaria
- Splenomegaly is almost invariable during the second week of illness

Treatment

1. Early IV quinine infusion is the mainstay of treatment of severe malaria. Levels should be monitored daily and dosage adjusted as appropriate. Complications include hypoglycaemia and tinnitus. Artemether should be considered in cases of likely quinine resistance.
2. A 2–3l exchange transfusion should be considered if the patient is severely ill or if parasitaemia levels >10–20%.
3. Careful attention must be paid to fluid and electrolyte balance and management of renal failure.
4. Treatment of hypoglycaemia, renal failure, coagulopathy, metabolic acidosis, seizures, ARDS, anaemia and hyperpyrexia follow conventional lines
5. Steroids are not recommended for cerebral oedema.
6. Suspect coincident Gram negative infection with circulatory collapse.

Drug dosage

First line	
Quinine	20mg quinine salt/kg IV over 4h, then 10mg/kg infusion over 4h, repeated 8-hrly until the patient can swallow, then tablets (10mg quinine salt/kg 8-hrly) to complete 7 days' treatment. Halve maintenance dose to 5mg salt/kg 8-hrly if continuing parenteral therapy for >48h.
Artemether	3.2mg/kg IM followed by 1.6mg/kg daily
Second line after asexual parasites eliminated	
Sulfadoxine 500mg/pyramethamine 25mg	3 tablets once
Doxycycline	200mg then 100mg daily for 7 days

See also:

Haemo(dia)filtration (1), p62; Haemo(dia)filtration (2), p64; Blood transfusion, p182; Fluid challenge, p274; Oliguria, p330; Acute renal failure—diagnosis, p332; Acute renal failure—management, p334; Generalised seizures, p372; Jaundice, p358; Anaemia, p400; Haemolysis, p404; Platelet disorders, p406; Infection—diagnosis, p480; Infection—treatment, p482; Pyrexia (1), p518;Pyrexia (2), p520

Rheumatic disorders

Rheumatoid arthritis

A debilitating arthritis that may present to intensive care through pulmonary involvement or through complications of treatment (e.g. renal failure, immunosuppression, bleeding disorders). Pleuro-pulmonary involvement may precede the arthritic symptoms and is more common in those with active rheumatoid disease and middle aged men. Care is required when intubating patients with rheumatoid arthritis since the neck joints may sublux.

Rheumatoid pleurisy

Rheumatoid pleurisy, often with effusion, is most common and is usually asymptomatic. However, effusions may be recurrent or chronic and may impede respiratory function. The effusion is an exudate, low in glucose and often high in cholesterol.

Rheumatoid lung

Rheumatoid lung is a diffuse interstitial pneumonitis with bi-basal fibrotic changes on the CXR. The condition may be difficult to distinguish from idiopathic pulmonary fibrosis and produces a restrictive pulmonary defect. The mainstay of treatment is early systemic steroid therapy, although chronic cases do not respond.

Systemic lupus erythematosis (SLE)

A non-organ specific autoimmune disease characterised by antinuclear antibodies with high titres of antidouble-stranded DNA antibodies. A vasculitis is prominent, although cutaneous and central nervous system involvement are not vasculitic. SLE may present to intensive care through pulmonary, renal or central nervous system involvement.

Renal failure

Renal failure is vasculitic in origin and may progress to end stage renal failure requiring long term dialysis. Early treatment with systemic steroids and immunosuppressives may halt disease progress.

Lupus pleurisy and pericarditis

Unlike rheumatoid pleurisy the pleural involvement in SLE is often painful and associated with large pleural effusions.

Pulmonary haemorrhage

Pulmonary haemorrhage is associated with renal failure and may be life threatening. Plasma exchange may be helpful.

Interstitial pneumonitis

Interstitial pneumonitis is uncommon in SLE. It is more likely that parenchymal infiltrates are infective in origin secondary to immunosuppressive therapy.

Pulmonary thromboembolic disease

Patients typically have a prolonged activated partial thromboplastin time due to circulating lupus anticoagulant. but are more prone to thrombotic episodes. Lupus anticoagulant is associated with anticardiolipin antibodies and a false positive VDRL. Recurrent pulmonary emboli may be associated with chronic pulmonary hypertension. Treatment is long term anticoagulation.

See also:

Vasculitides

Vasculitis should be suspected in any patient with multisystem disease, especially involving the lungs and kidneys.

Wegener's granulomatosis

A systemic vasculitis characterised by necrotising granulomas of the upper and lower respiratory tract, glomerulonephritis and small vessel vasculitis. Wegener's granulomatosis is associated with positive core antineutrophil cytoplasmic antibodies (c-ANCA), particularly granular with central attenuation on immunofluorescence. Intensive care admission is usually because of renal and/or pulmonary involvement.

Renal failure

Focal necrotising glomerulonephritis leads to progressive renal failure. Treatment with steroids and cyclophosphamide may give complete remission.

Upper airway disease

Most patients will have nasal symptoms including epistaxis, nasal discharge and septal perforation. Intensive care admission may be required rarely for severe epistaxis. Ulcerating lesions of the larynx and trachea may cause

subglottic stenosis. This is usually insidious but may present problems on attempted intubation.

Pulmonary involvement
Usually associated with haemoptysis, dyspnoea and cough with rounded opacities on the CXR. There may be cavitation. Nodules may be solitary. Alveolar haemorrhage may be life threatening. The mainstay of treatment is steroids and cyclophosphamide which may produce complete remission. Plasma exchange may be helpful.

Polyarteritis nodosa (PAN)
PAN is a necrotising vasculitis affecting small and medium sized muscular arteries. Intensive care admission may be provoked by renal failure, ischaemic heart disease, hypertensive crisis and bronchospasm, although true pulmonary involvement is uncommon. Diagnosis may be confirmed by mesenteric angiography or renal biopsy. Treatment involves renal replacement therapy, high dose steroids and cyclophosphamide.

Goodpasture's syndrome
Antiglomerular basement membrane (anti-GBM) antibodies bind at the glomerulus and alveolus. Patients present with a proliferative glomerulonephritis and haemoptysis. Diagnosis is confirmed by positive anti-GBM antibodies and renal biopsy. Treatment is with immunosuppressive therapy and plasma exchange.

See also:

Anaphylactoid reactions
Minor reactions to allergens (itching, urticaria) are common before a severe reaction occurs; any such history should be taken seriously and potential allergens avoided. Most reactions are acute in onset and clearly related to the causative allergen. However, some complement-mediated reactions may take longer to develop.

Clinical features

- Respiratory—laryngeal oedema, bronchospasm, pulmonary oedema, pulmonary hypertension
- Cardiovascular—hypotension, tachycardia, generalised oedema
- Other—urticaria, angio-oedema, abdominal cramps, rigors

Management

1. Stop all infusions and blood transfusions and withhold any potential drug or food allergen. Blood and blood products should be returned to the laboratory for analysis.

2. Start oxygen (FIO_2 0.6–1.0). If there is evidence of persistent hypoxaemia consider urgent intubation and mechanical ventilation.

3. If there is laryngeal obstruction, bronchospasm or facial oedema give IM or nebulised epinephrine and IV hydrocortisone. If there is not rapid relief of airway obstruction, consider urgent intubation or, in extremis, emergency cricothyroidotomy or tracheostomy. Persistent bronchospasm may require an epinephrine infusion, aminophylline infusion or assisted expiration (manual chest compression).

4. Hypotension should be treated with epinephrine IV/IM and rapid colloid infusion. Large volumes of colloid may be required to replace the plasma volume deficit in severe anaphylaxis.

   - Severe oedema may coexist with hypovolaemia.
   - Plasma volume has not been adequately replaced if the haemoglobin is higher than normal.
   - Hetastarch is the most appropriate fluid for colloid resuscitation unless the reaction is due to a hydroxyethyl starch.

5. Persistent hypotension should be treated with further epinephrine, hydrocortisone and colloid infusion guided by central venous pressure ± cardiac output monitoring. An epinephrine infusion may be required to overcome myocardial depression. The use of military antishock trousers or norepinephrine should be considered to divert blood centrally and increase peripheral resistance.

6. Urticaria requires chlorphenamine IV or PO depending on the severity of the reaction.

7. After control of the anaphylactoid reaction, advice should be sought from the immunology laboratory and appropriate samples taken for confirmation.

8. Reactions to long-acting drugs or fluids will require continued support (perhaps for many hours).

Drug dosages

Laryngeal oedema and bronchospasm

	Initial dose	Continued treatment
Epinephrine	0.3–0.5mg IM or 0.5mg nebulised	Start at 0.05µg/kg/min
Hydrocortisone	200mg IV	

Hypotension

	Initial dose	Continued treatment
Epinephrine	0.5–1.0mg IM or 0.05–0.2mg IV	Start at 0.05µg/kg/min
Hetastarch 6%	500ml	According to response
Hydrocortisone	200mg IV	200mg IV qds
Chlorphenamine		10mg IV tds

Urticaria

Chlorphenamine	10mg IV tds or 4mg PO tds
Hydrocortisone	50–100mg IV tds
Prednisolone	20mg PO daily

See also:

Ventilatory support—indications, p4; Endotracheal intubation, p36; Colloids, p180; Blood transfusion, p182; Inotropes, p196; Blood products, p252; Steroids, p262; Basic resuscitation, p270; Fluid challenge, p274

Trauma and Burns

Multiple trauma (1)

Such patients are admitted either after surgery or for close observation and medical management. The principles of management are to:

- Maintain or quickly restore adequate tissue perfusion and gas exchange
- Control pain
- Secure haemostasis and correct any coagulopathy

- Provide adequate nutrition
- Monitor closely and deal promptly with any complications

Circulatory management

- Patients are often cold and vasoconstricted on admission. This serves to camouflage concurrent hypovolaemia and compromise tissue perfusion.
- Adequate monitoring must be instituted at an early stage.
- Development of a persisting tissue oxygen debt has been shown to lead to subsequent multiple organ dysfunction which may not become clinically apparent for 3–7 days. Therefore, adequate perfusion must be restored promptly by repeated fluid challenges. Addition of a vasodilating agent, e.g. glyceryl trinitrate, may be beneficial.
- An increasing metabolic acidosis should prompt suspicion of inadequate resuscitation, covert haemorrhage or tissue necrosis. Myocardial depression or failure may also be implicated.

Respiratory management

- Consider the possibility of a fractured, unstable neck, especially in unconscious patients. This should be excluded by appropriate radiology and an expert opinion. Until then the neck should be immobilised.
- If ventilated, ensure haemodynamic stability, removal of any metabolic acidosis, adequate rewarming and satisfactory gas exchange before attempting to wean. If the patient remains unstable, it is advisable to delay extubation in case urgent surgery is required.
- If spontaneously breathing, give supplemental oxygen to provide adequate arterial oxygenation, encourage deep breathing to prevent atelectasis and secondary infection, and ensure sufficient analgesia, albeit not too much to suppress ventilatory drive.

Haematological management

- Maintain haemoglobin >7g/dl (higher with cardiorespiratory disease) to assist oxygen transport. Cross-matched blood should be readily available for secondary haemorrhage.
- Correct any coagulopathy with fresh frozen plasma, ± platelets, and, occasionally, other blood products (e.g. cryoprecipitate) or activated factor VII.

Peripheries

Injury to the limb may result in nerve injuries, obstruction of the vascular supply, or muscle damage which may lead to compartment syndrome and rhabdomyolysis. A high level of suspicion should be held and corrective surgery undertaken promptly if necessary.

See also:

Multiple trauma (2)

Analgesia

- Adequate analgesia is imperative to avoid circulatory instability and decreased chest wall excursion, especially following chest, abdominal or spinal trauma.
- Increased use of regional techniques (depending on absence of infection and coagulopathy) and patient-controlled analgesia has facilitated pain relief and weaning.
- Opiates are recommended for initial analgesia. Non-steroidals are particularly effective for bony pain though may occasionally precipitate coagulopathies, stress ulceration and renal failure.
- Agitation may be due to causes other than pain, e.g. infection, intracranial lesion.

Nutrition

Early nutrition has been shown to reduce post-operative complications. This should ideally be enteral, an approach

which has been demonstrated to be safe, even after abdominal laparotomy for trauma.

Infection

- Depending on the site of trauma, the type of wound (open/closed, clean/dirty), and the need for surgery, prophylactic tetanus and antibiotic cover varying from 1 dose to 1–2 weeks may be needed.

- The trauma patient is at high risk of developing secondary infection, in particular chest, wound sites, intravascular catheter insertion sites, post-abdominal trauma, intra-abdominal abscesses. Preventive measures and strict infection control should be undertaken.

- Intravascular catheters inserted during emergency resuscitation under non-sterile conditions should be replaced.

Prophylaxis

- Attention should be paid to pressure areas; this may involve the use of specialised mattresses or support beds.

- Clear instructions should be obtained from the surgeon regarding care of the wound and drain sites.

- Especially after orthopaedic procedures on the pelvis and lower limb, or if the patient will remain immobilised, heparin prophylaxis against deep venous thrombosis should be instituted.

Review

- Regular review of the patient is necessary to ensure complications are detected and dealt with promptly. This may require repeat laparotomy, ultrasound or CT scanning.

- Later complications include pancreatitis, acalculous cholecystitis, and multiple organ dysfunction (including ARDS).

See also:

Head injury (1)

The head may be injured with or without significant trauma to other parts of the body. Priority in management of the multiply injured patient must be placed on securing adequate gas exchange and circulatory resuscitation, and dealing with any life-threatening injury, e.g. an arterial injury, before definitive treatment for head injury.

The patient will usually be admitted to the ICU after CT scanning has identified the extent of injury. The neck should also be imaged by CT, particularly if the patient is ventilated. It is also likely that surgery will have been undertaken for any significant space-occupying lesion or for elevation of a depressed fracture.

General management

- An unstable neck fracture should be assumed until excluded by an expert opinion and appropriate investigations.

- Most head injury patients admitted to non-neurosurgical ICUs will have diffuse or local brain injury for which a non-operative approach has been adopted. The Regional Neurosurgery Centre should be contacted if raised intracranial pressure is present as local policy may encourage early bone flap decompression or referral for invasive monitoring (e.g. intracranial pressure, jugular venous bulb O_2 saturation).

- If a basal skull fracture is suspected (e.g. X-rays, rhinorrhoea, otorrhoea), avoid nasal insertion of feeding or endotracheal tubes.

- Deterioration in conscious level, developing neurological deficits or focal signs (e.g. unilateral pupillary dilatation) should prompt urgent repeat CT scanning for late complications, e.g. subdural haematoma.

Complications

- Actively manage raised intracranial pressure.

- Actively treat seizures with anticonvulsants to prevent further hypoxaemic cerebral damage, reduce cerebral oxygen requirements and ICP. The patient should be loaded with IV phenytoin as prophylaxis against further fits. Consider additional causes such as hypoglycaemia, development of a new space-occupying lesion, recreational drugs and infection.

- Diabetes insipidus suggests hypothalamic injury and carries a poor prognosis. Desmopressin 1–4µg IV should be given daily to maintain urine output of 100–150ml/h.

- Actively manage hyperpyrexia. Some studies show long-term benefit from induced hypothermia but this needs to

be aggressively instituted as early as possible after the injury to be effective.

- Actively manage hyperglycaemia with insulin, and avoid hypoglycaemia.

Key papers

Rovlias A, Kotsou S. The influence of hyperglycemia on neurological outcome in patients with severe head injury. Neurosurgery 2000; 46:335–42 Clifton GL, Miller ER, Choi SC et al. Lack of effect of induction of hypothermia after acute brain injury. N Engl J Med 2001; 344:556–63

See also:

Anticonvulsants, p242; Neuroprotective agents, p244; Generalised seizures, p372; Intracranial haemorrhage, p376; Raised intracranial pressure, p832; Multiple trauma (1), p500; Multiple trauma (2), p520; Head injury (2), p506; Spinal cord injury, p508

Head injury (2)

Analgesia

- Adequate analgesia (usually opiates) must be given to the head-injured patient as pain and agitation will increase intracranial pressure, thereby causing a secondary insult.
- Short-acting sedation should be used as this enables rapid assessment of the underlying conscious level and any focal neurological deficit.

Respiratory management

- Aggressive hyperventilation is no longer recommended apart from short-term management of raised intracranial pressure. If ventilated, aim to maintain the $PaCO_2$ at 3.5–4kPa.
- Face or neck injuries may have required emergency cricothyroidotomy or tracheostomy to obtain a patent airway. If orotracheally intubated, ensure local swelling has subsided (nasendoscopy, air leak around deflated cuff) before extubation.
- Severe agitation and confusion may last for several weeks; this will often delay weaning and extubation. Judicious sedation, e.g. with chlorpromazine, may be necessary.

Circulatory management

- Hypotension should be avoided with adequate fluid resuscitation ± vasopressor therapy.
- Elevated blood pressures may be tolerated unless excessive.
- β-blockers may be useful in reducing the myocardial effects of excessive catecholamine levels.

Other drug therapy

- Antibiotic prophylaxis is not routinely recommended.
- High-dose steroid therapy has not yet been shown to be beneficial.
- Trials of other neuroprotective agents, e.g. free radical scavengers, have also failed to show benefit.

Indications for consideration of intracranial pressure monitoring

Indications

- GCS ≤8 and any abnormality on CT scan
- GCS ≤8 and a normal CT scan but any two of the following:

  Age >40 years

  Hypotension

  Decerebrate posturing

- GCS >8 but:

  Requiring general anaesthesia for treatment of other injuries

  Requiring treatment likely to increase ICP, e.g. high levels of PEEP

Contraindications

- Coagulopathy

- Infection?

ICP monitoring should be continued:

- As long as the ICP is elevated

- During active management of ICP

- For up to 3 days in the absence of significant elevation

Spinal cord injury

Spinal injury, with or without damage to the cord, may be apparent soon after admission to hospital; however, deterioration may occur, requiring a high index of suspicion and careful monitoring.

Immobilisation

- The spine should be immobilised until a senior surgical/orthopaedic opinion has confirmed that no unstable fracture is present, both radiologically and clinically.

- Place a hard cervical collar if a neck fracture is possible. This does not stabilise the spine; either skull traction or operative stabilisation will be needed for an unstable fracture.

- Move the patient by 'log-rolling' or straight-lifting, using at least four staff members. Exercise care with neck manipulation; intubation should be performed by an experienced operator.

Circulatory instability

- So-called 'spinal shock' may occur with marked hypotension due to sympathetic outflow disturbance. Hypovolaemia should be excluded first. Consider damage to other organs/vessels, e.g. spleen, aorta.

- Vasopressor therapy may be necessary if evidence of tissue hypoperfusion persists, e.g. oliguria, metabolic acidosis.

- Postural hypotension and circulatory instability (including symptomatic bradycardia) is commonplace for the first few weeks. Autonomic dysfunction affects 50% of cervical and high thoracic cord injuries.

Respiratory management

- High cervical cord injury above C5 results in loss of diaphragmatic function, whereas above C8 can result in loss of intercostal function. This may compromise or prevent breathing and weaning from IPPV.

- When able, the patient should be managed in an upright posture.

- Atelectasis is common and requires regular physiotherapy.

- Early tracheostomy may facilitate support and comfort.

General measures

- Carefully monitor neurological function to enable early detection of spinal cord compression and referral for urgent remedial surgery.

- Give LMW heparin SC for thromboembolism prophylaxis.

- The incidence of stress ulceration is high. Ideally, enteral nutrition should be instituted at an early stage though this may prove unsuccessful. Drugs (e.g. sucralfate, H_2 blockers) may be needed.

- Enteral feeding may be difficult to institute initially as gastric distension and paralytic ileus is common following spinal cord injury. A NG tube should be inserted for gastric decompression. An enterostomy may eventually be needed to enable long-term feeding.

- Bowel and bladder function may be deranged. Long-term silastic bladder catheters and regular laxative and enema therapy should be instituted at an early stage.

- Special care is needed to prevent pressure sores.

- Institute regular exercises to prevent contractures.

- Psychological support for patient and family is crucial, particularly if long-term disability is likely.

- High-dose steroid therapy may be beneficial if started within 8h, though this still remains controversial.

- Hyperbaric oxygen therapy is of unproved benefit.

- After spinal injury, muscle relaxants may cause severe hyperkalaemia.

- Steroids have been shown to be useful but this remains controversial.

Key trial
Bracken MB, et al. Administration of methylprednisolone for 24 or 48 hours or tirilazad mesylate for 48 hours in the treatment of acute spinal cord injury. Results of the Third National Acute Spinal Cord Injury Randomized Controlled Trial. National Acute Spinal Cord Injury Study. JAMA. 1997; 277:1597–604

See also:
Special support surfaces, p86; Blood pressure monitoring, p110; H_2 blockers and proton pump inhibitors, p218; Sucralfate, p220; Anticoagulants, p248; Steroids, p262; Fluid challenge, p274; Hypotension, p312; Acute weakness, p368; Metabolic acidosis, p434; Multiple trauma (1), p500; Multiple trauma (2), p502; Head injury (1), p504; Head injury (2), p506

Burns—fluid management
Major thermal injuries (i.e. >20% body surface area) are admitted to an intensive care unit, usually specialising in the management of burns, for meticulous attention to fluid resuscitation, prevention of infection, and the frequent need for mechanical ventilation.

Monitoring

- The fluid loss from major burns requires careful assessment of intravascular volume status. The traditional markers of fluid resuscitation in burns of central venous pressure, urine output and haematocrit are generally inadequate.

- Either invasive or non-invasive cardiac output monitoring is needed for accurate titration of fluid. This is particularly applicable in the presence of a hyperdynamic, vasodilated circulation which often commences within 1–2 days. Although infection is not necessarily present, vasopressor therapy may be needed to maintain adequate systemic blood pressures.

- Pulmonary artery and central venous catheters should not be inserted through affected skin areas if at all possible.

- Insertion of intravascular catheters, urinary catheters and NG tubes should be carried out soon after admission as rapid onset swelling within a few hours may make these procedures impossible.

Fluid management

- The extent of injury will have been estimated by plastic surgeons who will also determine the proportion of full thickness dermal injury to calculate the approximate fluid resuscitation required.

- Fluid resuscitation in the UK often follows the Mount Vernon (albumin-based) formula while the Parkland (crystalloid-based) formula is often used in the US. Colloids may reduce oedema at non-burn sites and restore blood volume faster than crystalloids.

- These formulae only provide an approximate guide and frequently underestimate losses both into the interstitial spaces and through the lost skin barrier. Evaporative losses are approximately 2ml/kg/h. Water losses may be increased if wounds are not covered. Losses increase further with inhalation injury.

- Overzealous fluid infusion should be avoided to minimise oedema.

- The increased permeability and fluid leak phase lasts approximately 1–2 days. After 2–5 days, a diuretic phase usually commences when excess tissue fluid is lost and the body swelling reduces.

- Electrolyte levels (especially K^+ and Mg^{2+}) can fluctuate widely in both periods requiring monitoring and replacement as necessary.

- Though some haemolysis may occur, blood transfusion requirements are usually low, but debridement will result in major blood loss often requiring major transfusion (>8–10 units). A coagulopathy will often occur, in part due to a dilutional effect of the albumin infusion.

Fluid resuscitation regimen (adapted from Mount Vernon formula)
Note: this regimen should be used as a guide only.

1. Divide first 36h from the time of burn into six consecutive periods of 4, 4, 4, 6, 6 and 12h. For each period give 0.5ml 4.5–5% albumin × body wt [kg] × %burn

2. Give blood as necessary to maintain haemoglobin >10g/dl.

3. Commence enteral nutrition as soon as possible

4. Give 1.5–2ml/kg/h 5% glucose

5. Reassess cardiorespiratory variables and urine output at frequent intervals to determine whether volume replacement is inadequate or excessive. Adjust fluid input as necessary.

See also:

Blood pressure monitoring, p110; Central venous catheter—use, p114; Colloid osmotic pressure, p172; Crystalloids, p176; Colloids, p180; Basic resuscitation, p270; Fluid challenge, p274; Hypotension, p312; Oliguria, p330; Burns—general management

Burns—general management

Surgery

- Escharotomy may be needed on hospital admission to affected limbs, as well as to the neck and/or chest if a circumferential burn is present.

- Debridement of necrotic tissue is often begun within the first few days as early grafting is associated with improved outcome.

  Coverage is obtained using either split skin grafts from the patient's own unaffected skin, donor skin grafts or even experimental 'skin'.

  Blood loss may be rapid and massive, e.g. 100ml per 1% of body surface grafted.

Wound care

- Early application of dressings and Flamazine (silver sulphadiazine) cream which has anti-bacterial properties against Gram negative bacteria may usefully prevent secondary infection.

- Early grafting often takes place within the first 2–3 days to provide a skin protective barrier.

Nutrition

- Enteral nutrition should be commenced soon after admission as studies have shown that early enteral nutrition improves outcome.

- Target intake is protein of 1g/kg + 2g/%burn and a calorie intake of 20Cal/kg + 50Cal/%burn.

Infection

- Prophylactic antibiotics are often not given to burn patients.

- Body temperature rises on day 1–2 as high as 40°C, may persist for several days and does not indicate secondary infection.

- Likely infecting agents include streptococci, staphylococci and Gram negative bacteria such as *Pseudomonas*. Appropriate antibiotic treatment should be given as indicated.

Other considerations

- Any suspected inhalation injury should be diagnosed and treated.

- Ensure adequate analgesia (opiates). Ketamine is a useful anaesthetic as it has analgesic properties in addition.

- Tetanus toxoid should be given soon after hospital admission.

- Reduce heat and fluid losses by placing the patient on a heated air fluidised bed and by early coverage of burnt skin through application of occlusive dressings and placement of affected limbs in transparent plastic bags.

- Stress ulceration can usually be avoided through prompt resuscitation and early enteral nutrition.

- Pressure sores and contractures should be prevented by careful nursing and physiotherapy.

- Suxamethonium should be avoided from 5–150 days' post-burn because of the risk of rapid and severe hyperkalaemia.

- Increasing resistance to non-depolarising muscle relaxants may be seen.

- β-blockade has been associated with outcome improvement in children sustaining burn injury.

Physical Disorders

Hypothermia

Clinical features

- Above 33°C—shivering is usually marked in an attempt to correct body temperature.

- Below 33°C—neurological signs of dysarthria and slowness appear.

- Below 31°C—hypertonicity and sluggish reflexes with cardiovascular dysfunction become life threatening.

- Below 28°C—arterial pulses often become impalpable. Hypothermic rigidity is difficult to distinguish from death.

- Prognosis depends on the degree and duration of hypothermia.

ECG changes

Sinus bradycardia is followed by atrial flutter and fibrillation with ventricular ectopics. The PR interval, QRS complex and QT interval are prolonged. Atrial activity eventually ceases. The 'J' wave is most often seen <31°C and ventricular fibrillation is common <30°C, giving way to asystole <28°C.

Complications

Hypoxaemia is common due to hypoventilation and ventilation–perfusion mismatch. Hypovolaemia and metabolic acidosis are common. Renal tubular damage may result from renal blood flow reduction. Acute pancreatitis, rhabdomyolysis and gastric erosions are common.

Management

1. Oxygen (FIO_2 0.6–1.0) to maintain SaO_2 >95%.

2. Fluid replacement with careful monitoring.

3. Rewarming—All hypothermic patients with no evidence of other fatal disease should be assumed fully recoverable. In the event of cardiac arrest full resuscitation should continue until the patient is normothermic (ventricular fibrillation is resistant to defibrillation between 28 and 30°C). The technique used for rewarming depends on the core temperature (measured with a low reading rectal thermometer) and the clinical circumstance.

Rapid central rewarming

In cases where the temperature is <28°C (<33°C with acute exposure hypothermia), or where there is cardiac arrest, rapid rewarming may be achieved by peritoneal dialysis, gastric or bladder lavage with warmed fluids. These techniques may achieve rewarming rates of 1–5°C/h. Active surface rewarming with a heated blanket or warm air blanket can achieve rates of 1–7°C/h and is less invasive. Haemodynamic changes may be dramatic during active rewarming, requiring careful monitoring and support. If extracorporeal rewarming is available, rates of 3–15°C/h may be achieved with the addition of cardiovascular support.

Spontaneous rewarming

Spontaneous rewarming proceeds at a rate inversely proportional to the duration of hypothermia. With good insulation (space blanket), rewarming rates of 0.1–0.7°C/h can be achieved. Core temperature may fall during spontaneous rewarming as cold blood is returned from the periphery to the central circulation.

Causes of hypothermia

- Coma and immobility

- Cold water immersion

- Exposure
- Hypothyroidism
- Hypopituitarism
- Sepsis
- Erythroderma

See also:

Ventilatory support—indications, p4; Endotracheal intubation, p36; Defibrillation, p45; Peritoneal dialysis, p66; ECG monitoring, p108; Basic resuscitation, p270; Cardiac arrest, p272; Fluid challenge, p274; Tachyarrhythmias, p316; Bradyarrhythmias, p318; Pancreatitis, p354; Thyroid emergencies, p446; Rhabdomyolysis, p528

Pyrexia (1)

Mechanisms underlying a rise in temperature are poorly understood. It reflects the balance between heat loss and heat production. There may be inability to lose heat (e.g. high ambient temperature), 'thermostat' dysregulation within the hypothalamus or increased heat generation (e.g. due to mitochondrial uncoupling). There is some laboratory evidence that a raised temperature may be beneficial in terms of white cell response, heat shock protein activation and mitochondrial protection. Septic patients presenting with a low temperature have a poorer prognosis.

An excessive temperature may be unpleasant to the patient (e.g. rigors), will increase metabolic rate and therefore oxygen demand, may induce excessive vasodilatation and salt and water loss. At very high temperatures, biochemical function is disrupted with altered enzyme function and increased cell breakdown (e.g. rhabdomyolysis).

Causes

Infection

The commonest cause in the ICU patient, though over-diagnosed. Main sites are chest and intravascular catheter sites. Urinary tract infections are difficult to diagnose in the presence of a urethral catheter. Similarly, the respiratory tract is routinely colonised with bacteria within a few days of ICU admission; differentiation between colonising and pathogenic bacteria is difficult. Seek malaria in patients who have visited endemic areas. Antibiotic therapy may itself be a cause of pyrexia.

Inflammation

Inflammation unrelated to infection will usually generate a pyrexic response, e.g. systemic inflammatory response syndrome, post-cardiac surgery, post-burns, post-myocardial infarction, vasculitis, glomerulonephritis, hepatitis, acalculous cholecystitis. Other than specific therapy, e.g. immnosuppression for vasculitis, management is generally symptom-orientated to include cooling.

Adverse drug reaction

Numerous drugs may induce an idiosyncratic pyrexia, including antibiotics, sedatives, paralysing agents, and amphetamines. Usually removal of the offending drug is sufficient but more active measures may have to be taken, including active cooling and dantrolene.

Adverse reaction to blood transfusion

This may be related to an immunological reaction to one of the cellular constituents, or to contamination with an organism, bacterial cell products or other pyrogen.

Ambient heating

Excessive heating or prevention of heat loss may cause pyrexia. Consider strong sunlight, excess temperature control settings on specialised beds or mattresses, and heat-retaining bed clothing.

Miscellaneous

Other causes of pyrexia include neoplasm and post-cerebral insult (e.g. head injury, cerebrovascular accident).

Key paper

Circiumaru B, et al. A prospective study of fever in the intensive care unit. Intensive Care Med 1999; 25:668–73.

Pyrexia (2)

At present, the optimal temperature to target in disease states is not known, other than cerebral insults where normo- or even hypothermia appears to offer neuroprotection by reducing cerebral metabolic rate. In other conditions it seems reasonable to accept mild pyrexia provided this is tolerated by the patient.

Principles of management

1. Diagnose then remove or treat the offending cause. For example, seek and treat infection, stop blood infusion and send discontinued bag to laboratory for analysis, use anti-inflammatory ± immunosuppressive agents for vasculitis.

2. Cooling aids symptomatic recovery, reduces metabolic rate and lowers pressor requirements:

   - Increase evaporative losses, e.g. tepid sponging, wet sheets, ice packs
   - Increase convective losses, e.g. fanning to improve air circulation
   - Antipyretics, e.g. paracetamol, aspirin, chlorpromazine
   - More aggressive cooling if temperature >40°C
   - Aim to lower temperature to <38.5°C then reassess.

See also:

Hyperthermia

Hyperthermia is defined as a core temperature above 41°C.

Clinical features

- Delirium and seizures are associated with temperatures of 40–42°C
- Coma is associated with temperatures above 42°C
- Tachycardia
- Tachypnoea
- Salt water depletion
- Rhabdomyolysis
- Disseminated intravascular coagulation
- Heart failure with ST depression and 'T' wave flattening

Causes

- Hyperthermia may be an extreme form of pyrogen-induced fever associated with infection, inflammation, neoplasm or cerebrovascular accident.
- Heat stroke is associated with severe exercise in high environmental temperatures and humidity. There may be excess clothing or hypovolaemia reducing the body's ability to dissipate heat production.
- Malignant hyperthermia is a drug-induced myopathy associated with a hereditary calcium transfer defect in patients receiving volatile anaesthetics, muscle relaxants, antidepressants, alcohol or Ecstasy. Heat production is increased by muscle catabolism, spasm and peripheral vasoconstriction.
- The neuroleptic malignant syndrome is a drug-induced hyperthermic syndrome secondary to phenothiazines or butyrophenones. It is associated with muscle rigidity, akinesia, impaired consciousness and autonomic dysfunction and continues for 1–2 weeks.

Management

1. Rapid cooling should be instituted when temperatures exceed 41°C.
2. Supportive treatment includes fluid replacement and seizure control.
3. Clothing should be removed and patients should be nursed in a cool environment.
4. Surface cooling may be achieved with a fan, tepid sponging, wet sheets, ice packs or a cool bath.
5. Handling should be minimised and active cooling measures should be stopped when the core temperature is <39°C.
6. Internal cooling may be considered by gastric lavage or peritoneal lavage using cooled fluids.
7. Phenothiazines may be used to reduce temperature and prevent shivering (not in neuroleptic malignant syndrome).

8. Muscle relaxants should be used if the patient is ventilated.

9. For malignant hyperthermia the offending drug should be stopped and dantrolene 1mg/kg given IV every 5min to a maximum dose of 10mg/kg.

10. Mechanical ventilation with high FIO_2 and treatment of hyperkalaemia are required.

11. The neuroleptic malignant syndrome is treated by stopping the offending drug, giving dantrolene as above, and dopamine agonists (e.g. L-dopa or bromocriptine).

See also:

Ventilatory support—indications, p4; Blood pressure monitoring, p110; Coagulation monitoring, p156; Colloids, p180; Sedatives, p238; Muscle relaxants, p240; Basic resuscitation, p270; Fluid challenge, p274; Hypotension, p312; Agitation/confusion, p370; Generalised seizures, p372; Metabolic acidosis, p434; Thyroid emergencies, p446; Amphetamines including Ecstasy, p462; Pyrexia (1), p518; Pyrexia (2), p520; Rhabdomyolysis, p528; Post-operative intensive care, p534

Electrocution

The effects of electrocution are due to the effects of the current and the conversion of electrical energy to heat energy on passage through the tissues. Important factors are:

- Energy delivered—heat = amperage^2 × resistance × time, i.e. the amperage is the most important determinant of heat production.

- Resistance to current flow–tissues are resistant to current flow in the following decreasing order: bone, fat, tendon, skin, muscle, blood vessels, nerves. A high skin resistance and short duration of contact concentrate the effects locally. However, skin contaminants, moisture and burning reduce resistance.

- Type of current—alternating current is more dangerous than direct current. Tetanic muscle contractions may prevent the victim from releasing the current source whereas the single, strong muscle contraction with direct current often throws the victim clear. Alternating current is more likely to reach central tissues with consequent sustained apnoea and ventricular fibrillation (with as little as 50–100mA for 1–10ms).

- Current pathway—cardiorespiratory arrest is more likely the closer the contact is with the chest and heart.

Lightening strike differs from contact electrocution in that high intensity, ultra-short duration of current may produce cardiac arrest with little tissue destruction.

Clinical features

- Tachyarrhythmias—including ventricular tachycardia and fibrillation.
- Asystole—more likely with high current (>10A).
- Myocardial injury—heat injury, coronary artery spasm, arrhythmias, myocardial spasm.
- Respiratory arrest—tetanic contraction of the diaphragm, arrhythmias, cerebral medullary dysfunction.
- Trauma—tetanic muscle contraction, falling or being thrown clear.
- Burns—to skin and internal tissues.

Management

Most severe electrical injuries require urgent field treatment prior to hospital admission.

1. The first priority is to ensure that the source of the electrical injury is not a hazard to rescuers.

2. Management of cardiorespiratory arrest.

3. Prevention of further injury, e.g. spinal protection, removal of smouldering clothes

After hospital admission and restoration of the circulation management is directed towards the complications.

1. Maintain ventilatory support.

2. Management of hypovolaemia associated with burn injury. Fluid requirements are usually greater than for victims of thermal burns and require close monitoring.

3. Check cardiac enzymes for degree of myocardial injury. Treat heart failure and/or arrhythmias as indicated.

4. Management of rhabdomyolysis and covert compartment syndrome.

5. Surgical debridement of necrotic tissue and fixation of bony injury.

Near-drowning

Following near-drowning the major complications are lung injury, hypothermia and the effects of prolonged hypoxia. Although hypothermia bestows protective effects against organ damage, rewarming carries particular hazards.

Pathophysiology

Prolonged immersion usually results in inhalation of fluid; however, 10–20% of patients develop intense laryngospasm leading to so-called 'dry drowning'. Traditionally, fresh water drowning was considered to lead to rapid absorption of water into the circulation with haemolysis, hypo-osmolality and possible electrolyte disturbance whereas inhalation of hypertonic fluid from sea water drowning produced a marked flux of fluid into the alveoli. In practice, there seems to be little distinction between fresh and sea water as both cause loss of surfactant and severe inflammatory disruption of the alveolar-capillary membrane leading to an ARDS-type picture. Initially, haemodynamic instability is often minor. A similar picture often develops after 'dry drowning' and subsequent endotracheal intubation.

Acute hypothermia often accompanies near-drowning with loss of consciousness and haemodynamic alterations.

Management

1. Oxygen—FIO_2 0.6–1 should be given, either by face mask if the patient is spontaneously breathing, or via mechanical ventilation. Comatose patients should be intubated. Early CPAP or PEEP may be useful.

2. Bronchospasm is often present and may require nebulised β_2 agonists, and either nebulised or SC epinephrine.

3. Fluid replacement should be directed by appropriate monitoring. Inotrope therapy may be necessary if hypoperfusion persists after adequate fluid resuscitation. Intravascular fluid overload is uncommon and the role of early diuretic therapy with a view to lowering intracranial pressure is controversial. Haemolysis may occur and require blood transfusion.

4. Arrhythmias may arise secondary to myocardial hypoxia, hypothermia and electrolyte abnormalities. These should be treated conventionally.

5. Metabolic acidosis may be profound, but sodium bicarbonate therapy is rarely indicated as the acidosis will usually correct on restoration of adequate tissue perfusion.

6. Electrolyte abnormalities are usually minor and should be managed conventionally.

7. Rewarming follows conventional practice; cardiopulmonary bypass may be considered if core temperature is <30°C. Cardiopulmonary resuscitation including cardiac massage should be continued until normothermia is achieved.

8. Cerebral protection usually follows raised intracranial pressure protocols though, as mentioned above, the role of diuretic therapy and fluid restriction is controversial. Signs of brain damage such as seizures may become apparent and should be treated as they arise.

9. Antibiotic therapy (e.g. clindamycin, or cefuroxime plus metronidazole) should be given if strong evidence of aspiration exists. Otherwise, take specimens and treat as indicated.

10. Decompress the stomach using a nasogastric tube to lessen any risk of aspiration. Enteral feeding can be initiated afterwards.

Rhabdomyolysis

Breakdown of striated muscle which may result in compartment syndrome, acute renal failure and electrolyte abnormalities (hyperkalaemia, hypocalcaemia, hyperphosphataemia).

Causes

- Trauma, especially crush injury

- Prolonged immobilisation, e.g. after fall, drug overdose

- Drugs, e.g. opiates, Ecstasy
- Hyperpyrexia
- Vascular occlusion (including lengthy vascular surgery)
- Infection
- Burns/electrocution
- Congenital myopathy (rare)

Diagnosis

- Suggested by disproportionately high serum creatinine compared to urea (usual ratio is approximately 10μmol:1mmol).
- Raised creatine kinase (usually >2000IU/l).
- Myoglobinuria—this produces a positive urine dipstick to blood; laboratory analysis is required to confirm myoglobin rather than blood or haemoglobin. The urine is usually red or black but may appear clear despite significant rhabdomyolysis.

General management

- Prompt fluid resuscitation.
- Hypocalcaemia should not be treated unless the patient is symptomatic; administered calcium may form crystals with the high circulating phosphate.
- Hyperkalaemia may be resistant to medical management and require urgent haemodialysis or haemo(dia)filtration.

Compartment syndrome

- Suspect if limb is tender or painful and peripheries are cool. Loss of peripheral pulses and tense muscles are late signs.
- Manometry in muscle compartments reveal pressures >20–25mmHg.
- Arm, legs and buttock compartments may be affected.
- Management involves either prophylactic fasciotomies if at high risk or close monitoring (including regular manometry) with decompression if pressures exceed 20–25mmHg.
- Fasciotomies may result in major blood loss.

Renal failure

- Renal failure is thought to be produced by a combination of free radical injury, hypovolaemia, hypotension and, possibly, myoglobin blocking the renal tubules.
- Renal failure may be prevented by prompt rehydration and a forced alkaline diuresis with 6–10l 0.9% saline/day for 3–5 days, aiming to produce an equivalent amount of urine. The urinary pH should be maintained ≥6 and blood pH <7.5 using up to 500ml/h 1.24% sodium bicarbonate solution to increase urinary excretion of myoglobin. Furosemide and/or mannitol may be needed to avoid fluid overload and potassium, sodium, calcium and magnesium levels regularly monitored and managed as appropriate.
- If renal failure is established, dialysis or filtration techniques will be required, usually for a period of 6–8 weeks.

Key paper
Better OS, Stein JH. Early management of shock and prophylaxis of acute renal failure in traumatic rhabdomyolysis. N Engl J Med 1990; 322:825–9

See also:
Haemo(dia)filtration (1), p62; Haemo(dia)filtration (2), p64; Peritoneal dialysis, p66; Urinalysis, p166; Sodium bicarbonate, p178; Diuretics, p212; Oliguria, p330; Acute renal failure—diagnosis, p332; Acute renal failure—management, p334; Poisoning—general principles, p452; Amphetamines including Ecstasy, p462; Cocaine, p464; Multiple trauma (1), p500; Multiple trauma (2), p502; Burns—fluid management, p510; Burns—general management, p512; Hyperthermia, p522; Electrocution, p524

Pain and Post-operative Intensive Care

Pain

Pain results from many insults, e.g. trauma, invasive procedures, specific organ disease and inflammatory processes. Pain relief is necessary for physiological and psychological reasons:

- Anxiety and lack of sleep.

- Increased sympathetic activity contributing to an increased metabolic demand.

- The capacity of the circulation and respiratory system to meet the demands of metabolising tissues may not be adequate.

- Myocardial ischaemia is a significant risk.

- The endocrine response to injury is exaggerated with consequent salt and water retention.

- Physiological attempts to limit pain may include immobility and muscle splinting and consequent reductions in ventilatory function and cough.

Pain perception

The degree of tissue damage is related to the magnitude of the pain stimulus. The site of injury is also important; thoracic and upper abdominal injury is more painful than injury elsewhere. However, the perception of pain is dependent on other factors, e.g. simultaneous sensory input, personality, cultural background and previous experiences of pain.

Management of pain

Systemic analgesia

- Opioid analgesics form the mainstay of analgesic drug treatment in intensive care.

- Small, frequent IV doses or a continuous infusion provide the most stable blood levels. Since the degree of analgesia is dependent on blood levels it is important that they are maintained.

- Higher doses are required to treat rather than prevent pain.

- The dose of drug required for a particular individual depends on their perception of pain and whether tolerance has built up to previous analgesic use.

- The use of non-opioid drugs may avoid the need for or reduce the dose required of opioid drugs. This includes paracetamol and non-steroidals, ketamine and α_2-agonists such as clonidine and dexmedetomidine.

Regional analgesia

- Regional techniques reduce respiratory depression but require experience to ensure procedures are performed safely.

- Epidural analgesia may be achieved with local anaesthetic agents or opioids.

- Opioids avoid the vasodilatation and hypotension associated with local anaesthetic agents but do not produce as profound analgesia.

- The combination of opioid and local anaesthetic is synergistic.

- Intravenous opioids should be avoided or close monitoring should continue for 24h after cessation of epidural opioids due to the potential for late respiratory failure. Sample regimens are shown opposite.

- Local anaesthetic agents may be used to block superficial nerves, e.g. intercostal nerve block with 3–5ml 0.5% bupivacaine plus adrenaline.

Non-pharmacological techniques

Adequate explanation, positioning and physical techniques may all reduce drug requirements.

Regimens for epidural analgesia

Lumbar LA	10–15ml 0.5% bupivacaine followed by an infusion of 5–20ml/h 0.125% bupivacaine
Thoracic LA	4–6ml 0.5% bupivacaine followed by an infusion of 6–10ml/h 0.125% bupivacaine
Opioid	5mg morphine gives up to 12h analgesia
Combined	An infusion of 3–4ml/h 0.125% bupivacaine with 0.3–0.4mg/h morphine or 25–50µg/h fentanyl

See also:

Opioid analgesics, p234; Non-opioid analgesics, p236; Multiple trauma (1), p500; Multiple trauma (2), p502; Head injury (1), p504; Head injury (2), p506; Burns—general management, p512; Post-operative intensive care, p534

Post-operative intensive care

Patients may be admitted to the ICU after surgery, either electively (see opposite) or after unexpected peri-operative complications.

General care

- Ensure surgical and anaesthetic plan has been agreed, e.g. overnight ventilation, special precautions (e.g. wire cutters if mandible wired), movement allowed, haemodynamic targets, etc.
- Provide adequate analgesia.
- Ensure adequate rewarming.
- Maintain euglycaemia.
- Provide appropriate thrombosis prophylaxis.
- Blood gas, electrolyte and haemoglobin monitoring.

Post-operative respiratory problems

Common in those with pre-existing respiratory disease, especially with a reduced vital capacity or peak flow rate. Problems include:

- Exacerbation of chronic chest disease
- Retained secretions
- Basal atelectasis
- Pneumonia
- Upper airway problems, e.g. laryngeal oedema

Anaesthesia and surgery (especially upper abdominal surgery) reduce functional residual capacity, thoracic compliance and cough. There is reduced macrophage function and systemic inflammatory activation with infection and acute lung injury as possible consequences.

Therapeutic aims

Pre-operative preparation may help avoid some of the problems:

- Cessation of smoking for >1 week
- Bronchodilatation
- Respiratory muscle training
- Chest physiotherapy
- Avoidance of hypovolaemia in the nil-by-mouth period

Post-operative clearance of secretions and maintenance of basal lung expansion are very important. These require effective analgesia and chest physiotherapy. Consider early use of non-invasive ventilation if spontaneously breathing but requiring high FIO_2. Mechanical ventilation assists basal expansion and secretion clearance where anaesthetic recovery is expected to be prolonged or where surgery ± pre-existing disease increase the risk of secretion retention and atelectasis. Ensure a patent airway prior to extubation where intubation was difficult or after upper airway surgery.

Post-operative circulatory problems

- Prevention of hypovolaemia is crucial in avoiding inflammatory activation and, therefore, many post-operative complications.

- Haemorrhage is usually obvious and managed by resuscitation, correction of coagulation disturbance and surgery.

- Subclinical hypovolaemia is common postoperatively. Hypothermia and high catecholamine levels help to maintain CVP and BP despite continuing hypovolaemia. Avoiding reduced stroke volume or metabolic acidosis are the best indicators of adequate resuscitation.

- Post-operative fluid management requires a high degree of suspicion of hypovolaemia; fluid challenges with colloid should be used to confirm and treat hypovolaemia where there is any circulatory disturbance, metabolic acidosis or oliguria.

Reasons for elective ICU admission

- Airway monitoring: e.g. major oral, head and neck surgery

- Respiratory monitoring: e.g. cardiothoracic surgery, upper abdominal surgery, prolonged anaesthesia, previous respiratory disease

- Cardiovascular monitoring: e.g. cardiac surgery, vascular surgery, major abdominal surgery, prolonged anaesthesia, previous cardiovascular disease

- Neurological monitoring: e.g. neurosurgery, cardiac surgery with circulatory arrest

- Elective ventilation: e.g. cardiac surgery, major abdominal surgery, prolonged anaesthesia, previous respiratory disease

See also:

Ventilatory support—indications, p4; Endotracheal intubation, p36; Non-invasive respiratory support, p32; Chest physiotherapy, p48; Pulse oximetry, p90; Blood gas analysis, p100; ECG monitoring, p108; Blood pressure monitoring, p110; Central venous catheter—use, p114; Central venous catheter—insertion, p116; Cardiac output—thermodilution, p122; Cardiac output—other invasive, p124; Cardiac output—non-invasive (1), p126; Cardiac output—non-invasive (2), p128; Electrolytes $(Na^+, K^+, Cl^-, HCO_3^-)$, p146; Full blood count, p154; Coagulation monitoring, p156; Colloids, p180; Blood transfusion, p182; Bronchodilators, p186; Respiratory stimulants, p188; Opioid analgesics, p234; Non-opioid analgesics, p236; Sedatives, p238; Muscle relaxants, p240; Anticoagulants, p248; Coagulants and antifibrinolytics, p254; Fluid challenge, p274; Respiratory failure, p282; Atelectasis and pulmonary collapse, p284; Chronic airflow limitation, p286; Hypotension, p312; Oliguria, p330; Metabolic acidosis, p434; Hypothermia, p516; Pain, p532

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Obstetric Emergencies

Pre-eclampsia and eclampsia

The hallmark of pre-eclampsia is hypertension with proteinuria. It is considered mild if proteinuria is 0.25–2g/l and severe if >2g/l. Eclampsia is the same condition associated with seizures. They are associated with cerebral oedema and, in some cases, haemorrhage. A reduced plasma volume, raised peripheral resistance and disseminated intravascular coagulation all impair tissue perfusion, with possible renal and hepatic failure. Pulmonary oedema may occur secondary to increased peripheral resistance and low colloid osmotic pressure.

Management

Hypertensive crises and convulsions may continue for 48h post-partum, during which time close monitoring in a high dependency or intensive care area is essential.

Circulatory management

- High blood pressure is due to arteriolar vasospasm so controlled plasma volume expansion is essential as the first line treatment.

- A standard fluid challenge regimen may be used in the intensive care area with little risk of fluid overload.

- Oliguria may coexist with reduced plasma volume; controlled volume expansion is usually more appropriate than diuretic therapy.

- If plasma volume expansion fails to control hypertension, anti-hypertensives such as labetalol, nifedipine or hydralazine may be used.

Convulsions

- Convulsions are best avoided by good blood pressure control.

- Initial seizure control may be achieved with small doses of benzodiazepines.

- Magnesium sulphate is the treatment of choice for eclamptic convulsions. Magnesium levels should be monitored and kept between 2.5–3.75mmol/l. Above 3.75mmol/l toxicity with possible cardiorespiratory arrest may be seen.

- Prophylactic anticonvulsant therapy with magnesium may also be considered in pre-eclampsia.

- Excess sedation should be avoided due to the risk of aspiration although continued seizures may require elective intubation, mechanical hyperventilation and further anticonvulsant therapy.

Early fetal delivery

The definitive treatment for eclampsia is fetal delivery but the needs of the fetus must be balanced against those of the mother. If fetal maturity has been reached immediate delivery after control of seizures and hyper-tension is necessary.

Drug dosages

Labetalol	Start at 2mg/min IV or quicker if a rapid response is required. Labetalol is usually effective once 200mg has been given after which a maintenance infusion of 5–50mg/h may be continued.
Nifedipine	10mg SL is an often effective alternative, given every 20min if necessary.
Hydralazine	5–10mg by slow IV bolus, repeat after 20–30min. Alternatively, by infusion starting at 200–300μg/min and reducing to 50–150μg/min.
Magnesium	4g over 20min followed by 1–1.5g/h by intravenous infusion until seizures have stopped for 24h.

Key papers

Magpie Trial Collaboration Group. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. Lancet 2002; 359:1877–90

Which anticonvulsant for women with eclampsia? Evidence from the Collaborative Eclampsia Trial. Lancet 1995; 345:1455–63

See also:

Ventilatory support—indications, p4; Blood pressure monitoring, p110; Central venous catheter—use, p114; Central venous catheter—insertion, p116; EEG/CFM monitoring, p138; Coagulation monitoring, p156; Colloid osmotic pressure, p172; Colloids, p180; Hypotensive agents, p202; Anticonvulsants, p242; Fluid challenge, p274; Hypertension, p314; Generalised seizures, p372

HELLP syndrome

HELLP syndrome is a pregnancy related disorder associated with haemolysis, elevated liver function tests and low platelets. Criteria used for the diagnosis of HELLP are shown below.

- Microangiopathic haemolysis results from destruction of red cells as they pass through damaged small vessels.

- Hepatic dysfunction is characterised by periportal necrosis and hyaline deposits in the sinusoids. In some cases hepatic necrosis may proceed to hepatic haemorrhage or rupture.

- Thrombocytopenia results from increased platelet consumption, although prothrombin time and activated partial thromboplastin time are normal, unlike in DIC.

Clinical features

- Epigastric or right upper quadrant pain with malaise.

- Nausea and vomiting.

- Generalised oedema is usual but hypertension is less common. Presentation may occur post-partum.

Criteria for diagnosis of HELLP syndrome

Haemolysis

    Abnormal blood film

    Hyperbilirubinaemia

    LDH >600U/l

Elevated liver enzymes

    AST >70U/l

Thrombocytopenia

    Platelets <100 × 10^9/l

Management

- Priorities for management include basic resuscitation and exclusion of hepatic haemorrhage or ruptured liver. In the latter case an early Caesarean section and definitive surgical repair are urgent.

- Microangiopathic haemolysis and thrombocytopenia may respond to plasma exchange and fresh frozen plasma infusion.

- Platelet transfusions should be avoided unless there is active bleeding.

See also:

Post-partum haemorrhage

Usually due to incomplete uterine contraction after delivery, but may be due to retained products. The magnitude of haemorrhage may be severe and life threatening.

Resuscitation

The principles of resuscitation are the same as those applying to any haemorrhagic condition. Blood transfusion requirements may be massive and there may therefore be a need to replace coagulation factors. There may be significant retroplacental bleeding which may lead to underestimation of blood volume loss. It is safer to manage fluid and blood replacement with haemodynamic monitoring.

Aortic compression

Temporary reduction of haemorrhage may be achieved by compressing the aorta with a fist pushed firmly above the umbilicus, using the pressure between the fist and vertebral column to achieve compression. This manoeuvre may buy time while definitive surgical repair is organised.

Stimulated uterine contraction

Prostaglandin $F_{2\alpha}$ injected locally into the uterus or IM is an effective method of stimulating uterine contraction and may avoid the need for surgery.

Arterial occlusion

Angiographic embolisation or internal iliac artery ligation may avoid the need for hysterectomy in some cases. The disadvantages of these procedures include a significant delay in organisation and, in the latter case, the high failure rate.

See also:

Amniotic fluid embolus

- An uncommon but dangerous complication of childbirth.

- There is a high early mortality associated with acute pulmonary hypertension.

- The initial response of the pulmonary vasculature to the presence of amniotic fluid is intense vasospasm resulting in severe pulmonary hypertension and hypoxaemia.

- Right heart function is initially compromised severely but returns to normal with a secondary phase during which there is severe left heart failure and pulmonary oedema.

- Amniotic fluid contains lipid-rich particulate material which stimulates a systemic inflammatory reaction. In this respect the progress of the condition is similar to other causes of multiple organ failure with associated capillary leak and disseminated intravascular coagulation.

- Diagnosis is supported by amniotic fluid and fetal cells in pulmonary artery blood and urine, though this finding is not specific for embolus.

Management
Management is entirely supportive. If amniotic fluid embolism occurs prior to delivery urgent Caesarean section must be performed to prevent further embolisation.

Respiratory support
Oxygen (FIO$_2$ 0.6–1.0) must be provided. In many cases CPAP or mechanical ventilation will be required.

Cardiovascular support
Standard resuscitation principles apply with controlled fluid loading and inotropic support being started as required.

Haematological management
Management of the coagulopathy requires blood product therapy guided by laboratory assessment of coagulation times. In addition, some cases improve after treatment with cryoprecipitate, possible due to the effects of fibronectin replacement.

See also:

Death and the Dying Patient

Brain stem death
The correct diagnosis of brain stem death allows discontinuation of futile ventilation and enables potential retrieval of organs for donation. Diagnosis of brain stem death is usually followed by asystole within a few days. Before brain stem function testing can be performed to confirm the diagnosis the patient must have an underlying diagnosis compatible with brain stem death. They must be comatose and non-responsive for at least 6h and there should be a minimum of 2h following a cardiac arrest. There must be no hypothermia (temperature >35°C), evidence or suspicion of depressant drugs, significant metabolic abnormality or muscle relaxant effect. The performance of brain stem death tests should not proceed until relatives and all medical and nursing staff involved with the patient have had a chance to take part in discussions, although the test itself does not require consent. Cessation of mechanical ventilation is seen by many lay people as the final point of death. Clearly, this final step is easier if all are aware that it is to happen. If organ donation is considered, the transplant coordinator should be involved at an early stage.

Brain stem death testing
Procedures vary internationally. In the UK clinical assessment of brain stem reflexes must be performed by 2 doctors who have been registered for >5 years. An EEG is required in other countries.

Pupillary light reflex
Pupils should appear fixed in size and fail to respond to a light stimulus.

Corneal reflexes
These should be absent bilaterally

Pain response

There should be no cranial response to supraorbital pain.

Vestibulo-ocular reflexes

After confirming that the tympanic membranes are clear and unobstructed 20ml iced water is syringed into the ear. The eyes would normally deviate toward the opposite direction. Absence of movement to bilateral cold stimulation confirms an absent reflex.

Oculo-cephalic reflexes

Also called 'doll's eye' reflexes. With the eyelids held open, brisk lateral rotation of the head normally produces opposite rotation of the eyeball as if to fix the gaze on an object. This rotation is lost in brain stem death.

Gag reflex

The gag reflex is absent in brain stem death. However, the gag reflex is often lost in patients who are intubated.

Apnoea test

While the reflex assessments are being performed the patient should be pre-oxygenated with 100% oxygen. The ventilator is disconnected and 6l/min oxygen is passed into the trachea via a catheter. Apnoeic oxygenation can sustain SaO_2 for prolonged periods but there is an inevitable rise in $PaCO_2$ which should stimulate respiratory effort. After 3-15min of disconnection blood gas analyses are performed until $PaCO_2$ >6.7 kPa. Any respiratory effort negates the diagnosis of brain stem death.

See also:

Blood gas analysis, p100; EEG/CFM monitoring, p138; Urea and creatinine, p144; Electrolytes $(Na^+, K^+, Cl^-, HCO_3^-)$, p146; Toxicology, p162; Opioid analgesics, p234; Non-opioid analgesics, p236; Sedatives, p238; Muscle relaxants, p240; Cardiac arrest, p272; Hypoglycaemia, p438; Hypothermia, p516; Care of the potential organ donor, p552

Withdrawal and withholding treatment

This is arguably the most difficult and stressful decision that has to be made for the critically ill patient. Withdrawal involves reduction or cessation of vasoactive drugs and/or respiratory support. In some ICUs the patient is heavily sedated and disconnected from the ventilator. Withholding involves non-commencement or non-escalation of treatment, e.g. applying an upper threshold dose for an inotrope and/or not starting renal replacement therapy.

Before approaching the patient/family, there should ideally be a consensus among medical and nursing staff that quantity and/or quality of life are significantly compromised and unlikely to recover. Often, the patient's viewpoint is very well-defined and the carers may rue the fact that the discussion was not initiated earlier.

Ethnic, cultural and religious factors will influence both doctor and patient/family in the timing and frequency of such decisions. In some societies doctors have a more paternalistic approach with little involvement of patient and/or family in the decision-making process. Others are overly inclusive, sometimes to the point of excessively acquiescing to the family's demands despite obvious futility in continuing care. Clearly, a balance needs to be struck that serves the best interests of the patient. Although potentially awkward, the mentally competent patient should be involved in the most important decision affecting their life. This should be done as considerately as possible, avoiding unnecessary distress. A series of discussions over several days may be needed, allowing time to contemplate. Consensus is reached with >95% of patients/families by the third discussion.

It should be stressed to the patient and family that care is *not* being withdrawn/withheld but that pain relief, comfort, hydration and general nursing care are to be continued. Likewise, no decision is binding but can be amended depending on the patient's progress, e.g. moving from withholding to withdrawal, or re-institution of full treatment. A 'negotiated settlement' is often a useful interim compromise for families unable to accept a withdrawal decision, whereby limitation of treatment is instituted and subsequently reviewed

Relatives can sometimes be very distraught and, occasionally, irrational on discussing withdrawal/withholding. For many, this will be their first experience of the dying process in a loved family member. A number of other factors including guilt, anger and within-family disagreements may also surface. It should be stressed that the withdraw/withhold decision should not be left to the family alone as this is an unfair burden for them to carry. Rather, it is their passive agreement with a medical recommendation that is being sought. The emphasis of the discussion is to inform them of the likely outcome and to seek their view of what the patient would want. They need to be dealt with both sensitively and honestly, and they should not feel pressured to give instant decisions.

Discussions should involve the patient's nurse and other involved carers as appropriate. It should be accurately documented in the case notes to ensure good communication between caregivers and act as source data should subsequent complaints surface.

See also:

Communication, p564

Care of the potential organ donor

Patients with suspected brain stem death should be considered candidates for organ donation unless there is evidence of:

- Cancer (except primary central nervous system)
- HIV or hepatitis surface antigen positive
- High risk for HIV
- Uncontrolled sepsis
- Significant systemic disease
- Slow virus infection

The transplant co-ordinator should be contacted early (before the family are approached) to confirm likely suitability. If the family are amenable, the transplant co-ordinator will then initiate organ donation procedures. Do not reject those brain dead potential donors who, for example, have fully treated infections or acute renal failure without consultation with the transplant co-ordinator.

Management

1. Confirm brain stem death with appropriate testing.
2. Laboratory tests for blood group, HIV and hepatitis status and electrolytes.
3. Confirm organ donation is permissible by the coroner (or equivalent).
4. Maintain optimal cardiorespiratory status with fluid ± inotropes, optimal ventilation and physiotherapy. Diabetes insipidus should be treated with DDAVP.
5. Contact surgical and anaesthetic teams.

Organ suitability

- Kidneys—Age 4–70, acceptable U&E and creatinine
- Heart—Age 0–50, acceptable CXR and ECG
- Lungs—Age 0–50, acceptable CXR and blood gases
- Liver—Age 0–55, no alcohol or drug abuse, acceptable LFTs
- Corneas—Age 0–100, no previous intraocular surgery

The transplant co-ordinator will advise on other organ and tissue suitability, e.g. pancreas, trachea, bowel, skin.

P.553

See also:

Blood gas analysis, p100; Urea and creatinine, p144; Electrolytes

$(Na^+, K^+, Cl^-, HCO_3^-)$

, p146; Colloids, p180; Inotropes, p196; Vasopressors, p200; Fluid challenge, p274; Hypotension, p312

ICU Organisation and Management

ICU layout

The intensive care unit should be easily accessible by departments from which patients are admitted and close to departments which share engineering services. It is desirable that critically ill patients are separated from those requiring coronary care or high dependency care where a quieter environment is often needed. It is possible to provide intensive care and high dependency care in the same unit so long as patients can be separated within the unit. However, the differing requirements of these patients may limit such flexibility. The floor sizes given below represent a minimum guide.

Size

Intensive care bed requirements depend on the activity of the hospital with additional beds required for regional

specialties such as cardiothoracic surgery or neurosurgery. Very small (<6 beds) or very large (>14 beds) units may be difficult to manage although larger units may be divided operationally and allow better concentration of resources.

Patient areas

- Patient areas must provide unobstructed passage around the bed with a floor space of 26m^2 per bed. Curtains or screens are required for privacy.

- Floors and ceilings must be constructed to support heavy equipment (some pieces may weigh 1000kg).

- Doors must allow for passage of bulky equipment as well as wide beds.

- Every bed should have access to a wash hand basin.

- The specification should include 1 cubicle per 2 beds with 26m^2 floor area for isolation. Air conditioning should allow for positive and negative pressure control in cubicles and temperature and humidity control.

- Services must include adequate electricity supply (at least 28 sockets per bed) with emergency back-up supply. Oxygen (4), medical air (2) and suction (2) outlets must be available for every bed.

- The bed areas should have natural daylight and patients and staff should ideally have an outside view.

- Communications systems include an adequate number of telephones to avoid all telephones being in use at once, intercom systems to allow bed to bed communication and a system to control entry to the department.

- Computer networks should enable communication with central hospital administration and laboratory systems.

Other areas

Other areas include adequate storage space, dirty utility, clean utility, offices, laboratory, seminar room, cleaners' room, staff rest room, locker room, toilets, relatives' area, bedroom and interview room.

ICU staffing (medical)

Intensive care has evolved from the early success in simple mechanical ventilation of the lungs of polio victims to the present day where patients admitted to intensive care will usually have failure or dysfunction of one or more organ systems requiring mechanical support and monitoring. The intensive care unit should have dedicated consultant sessions with additional allocation for management, teaching and audit activities. These sessions should be divided between several intensive care specialists. In addition, the intensive care specialist should be supported by junior doctors in training who can provide 24h per day cover on a rota which provides adequate rest.

Required skills of intensive care medical staff

Management

Senior intensive care medical staff, assisted by senior nursing and pharmacy colleagues, command the primary responsibility for the financial management of the intensive care unit. It is through their actions that treatment of the critically ill is initiated and perpetuated; they are ultimately responsible for the activity of the unit and patient outcome.

Decision making

In the ICU most decisions are ultimately made by team consensus. Clinical decisions in the intensive care unit can be thought of under three categories: (i) decisions relating to common or routine problems for which a unit policy exists; (ii) decisions relating to uncommon problems requiring discussion with all ICU and non-ICU staff currently involved and (iii) decisions of an urgent nature taken by intensive care staff without delay.

Practical skills

Expertise in the management of complex equipment, monitoring procedures and performance of invasive procedures are required.

Clinical experience

Medical staff require experience in the recognition, prevention and management of critical illness, infection control, anaesthesia and organ support.

Technical knowledge

The intensive care specialist has an important role in the choice of equipment used in the intensive care unit.

Pharmacological knowledge

Drug therapy regimens are clearly open to the problems of drug interactions and, in addition, pharmacokinetics are often severely altered by the effects of major organ system dysfunction, particularly involving the liver and kidneys.

Teaching and training

The modern intensive care specialist has acquired a number of skills that cannot be gained outside the intensive care unit. It is therefore necessary to be able to provide this education to junior doctors in training for intensive care.

ICU staffing (nursing)

Critically ill patients require close nursing supervision. Many will require high-intensity nursing throughout a 24h period while others are of a lower dependency and can share nurses. In addition to the bedside nurses, the department needs additional staff to manage the day to day operation of the unit, to assist in lifting and handling of patients, to relieve bedside nurses for rest periods and to collect drugs and equipment. These additional nurses (or nurse assistants) can be termed the 'fixed nursing establishment' and the nature of their duties is such that they will usually be higher grade nurses. The bedside nurses are a 'variable establishment' and their numbers are dependent on activity such that more patients require higher numbers. Most departments fix their variable establishment by assuming an average activity.

Fixed establishment

In the UK providing 1 nurse per shift continuously requires 5.5 nurses. In addition staff handover, annual leave, study leave and sickness are usually calculated at 22% such that 1 additional nurse is required. Thus, the provision of 1 nurse in charge of each shift and 1 nurse to support the bedside nurses requires 11 nurses. In larger units there may be a need for additional support nurses.

Variable establishment

The same principles apply for the provision of bedside nurses. Thus, to provide 1:1 nursing for a bed requires 5.5 nurses and to provide 1:2 nursing requires 2.75 nurses. The total number required depends on the occupancy and the nurse to patient ratio for each occupied bed. One of the difficulties in staffing an intensive care unit relates to the variable dependency and occupancy. An average dependency weighted occupancy (average occupancy × average nurse to patient ratio) should be used to set the establishment of bedside nurses with additional nurses being drafted in from a bank or agency to cover peak demands.

Skill mix

Nursing skill mix is the subject of much controversy as the need for economy is balanced against the need for quality. As stated above the fixed nursing will usually be of higher grade since the role incorporates the administration of the unit and supervisory nursing. The bedside nurses will be made up of those who have received post-qualification training in intensive care and those who have not. The ratio of trained to untrained intensive care nurses should be of the order of 3:1 to facilitate in-service teaching.

Fire safety

Fires affecting the ICU are rare but are particularly difficult in that patients are not easily evacuated, yet their lives depend on services which fire may disrupt. Smoke, while dangerous to staff and the less critically ill patients who may be breathing spontaneously, is less of a problem to those on mechanical ventilation since their fresh gas supply is from outside the affected environment. It therefore follows that, in the event of fire, the priority is to ensure safety and means of escape for the staff first.

Control of smoke

Smoke and toxic gases are a common association with fire and may, in themselves, be flammable, particularly in association with high concentrations of oxygen. The main techniques for control of smoke include containment (e.g. fire-resisting walls, doors and seals) and dispersal (e.g. positive pressure air conditioning), the latter being used in patient areas. The possibility of flammable or toxic fumes should be considered when equipping and furnishing the intensive care unit.

Escape from fire

- Escape routes should be well marked and unobstructed.
- The nature of critical illness is such that not all patients can be evacuated.
- The staff should escape first by proceeding to the nearest exit away from the fire.
- Patients should be evacuated in the order of the least sick first.
- Evacuation of patients should be managed by someone trained in the use of breathing apparatus; in most cases this will be the fire brigade.
- If patients are to be evacuated they should be moved to a place of safety on the same floor as the intensive care unit. Patients should not be moved downstairs.
- In the majority of fires containment will reduce the need for full evacuation.

Preventing fire

- Automatic smoke or heat alarms should be provided in all areas.
- Cooking areas and laboratory areas must be separated from patient areas by fire doors.

- Fire doors are provided to protect staff and patients and should not be wedged open.

- If a closed door would compromise the care given to patients but is essential to separate fire compartments then an electro-mechanical device should hold the door open and be disabled by the fire alarm.

- Fire extinguishers of the appropriate types should be readily available and staff should be properly trained in their use.

Communication

Good communication is essential to the smooth running of the ICU. This includes communication between the ICU staff, patients, visiting professionals and relatives.

Patient communication

Critically ill patients may still be able to hear conversation despite sedation or apparent unconsciousness. Bedside discussions should take this into account and all procedures should be explained to the patient in simple terms before starting. The patient who is not competent to consent to treatment may appreciate verbal discussion or explanation.

Doctor–nurse communication

It is essential that the multidisciplinary approach to intensive care involves medical and nursing staff in decision making. Ward rounds are a forum for such interdisciplinary communication and the consultant leading the round should ensure that all present are truly involved. The plan for the day can be set on the ward round but is more likely to succeed if all involved in effecting the plan are involved in setting it. Similarly, all changes from the plan, whether due to unforeseen emergencies or due to failure of the patient to respond, should be fully discussed.

Communication with visiting teams

The intensive care staff should be responsible for the day to day care of critically ill patients, including coordinating the input from various non-ICU professionals involved in the management of patients and affecting the treatment plan. The admitting team should be involved in major decisions. Visiting medical staff should not see patients without being accompanied by a member of the intensive care medical staff.

Communication with relatives

Relatives are often overwhelmed by the environment of an intensive care unit, are worried about the patient and are easily confused by the information they are given about critically ill patients. Most communication should be face to face, avoiding lengthy discussions on the telephone. Where several people are imparting information, differences in emphasis or content destroy any chance of effective communication. It is essential that the bedside nurse is present when relatives are spoken to since there are often questions and concerns which crop up later and are directed to the nurse; it is worth remembering that the relatives have greater contact with the nurses and often build up a relationship with them. Where admitting teams need to communicate with relatives about a specific aspect of the illness the bedside nurse and, ideally, a member of the intensive care medical staff, should be present. Most interviews with relatives should be away from the bedside although it is often helpful to impart simple information at the bedside, particularly to demonstrate particular issues. Again it must be remembered that the patient may hear the conversation. While it is helpful to interview all relatives together this is not always practical, either because they cannot all be present at once or because they do not relate to each other. Information often changes when delivered second hand so it is better to communicate directly with various relatives separately in these circumstances.

Medicolegal aspects

The intensive care unit is a source of many medicolegal problems. Patients are often not competent to consent to treatment. They may be admitted following trauma, violence or poisoning, all of which may involve a legal process. Admission may also follow complications of treatment or medical mishaps occurring elsewhere in the hospital. The nature of critical illness is such that complications are common and litigation may follow.

Consent and agreement

Many procedures in intensive care are invasive or involve significant risk. The patient is often not competent to consent for such treatment and, in many countries, surrogate consent or assent cannot be legally given by the next-of-kin. It is important that the risks and benefits of the procedure are explained to the next-of-kin and that this discussion is documented in the case records. For major decisions, particularly those involving withdrawal or withholding of life-prolonging treatments, the patient should ideally be involved in discussions. If not feasible, relatives should be asked to give their view of what the patient would want in this situation.

Research presents consent problems in the critically ill and requires close ethical committee supervision.

Note-keeping

It is impossible to record everything that happens in intensive care in the patient's notes. The 24h observation chart provides the most detailed record of what has happened but summary notes are essential. Such notes must be factual without unsubstantiated opinions about the patient or about previous treatment. All entries must be timed and

signed. Records of ward rounds must record the name of the consultant leading the round. It must be remembered that the notes may be used later in legal proceedings. They may be used against you but, if well kept, will usually form the best defence. In the event of a medical mishap the episode should be clearly documented after witnessed explanation to relatives.

Dealing with the police

Most police enquiries relate to patients who are admitted after suspicious circumstances. While there is a duty to patient confidentiality it may be in the patient's interests to impart information about them. This may be with the consent of the patient or the next of kin. Written statements or verbal information may be requested. Any information given should avoid opinion and be strictly factual.

Dealing with the Coroner

The Coroner must be informed of any death where a death certificate cannot be issued. Death certificates can be issued where the death is due to a natural cause and the patient has been seen professionally by the doctor within 14 days prior to death. The table documents the conditions requiring the Coroner to be informed. Where there is any doubt the Coroner should be informed.

Deaths which must be informed to the Coroner

- Unidentified body
- No doctor attending within prior 14 days
- Death without recovery from anaesthesia
- Sudden or unexplained death
- Medical mishap
- Industrial accident or disease
- Violence, accident or misadventure
- Suspicious circumstances
- Alcoholism
- Poisoning
- Death in custody

Clinical governance

Clinical governance is a framework through which healthcare organizations are accountable for continuously improving the quality of their services and safeguarding high standards of care by creating an environment in which excellence in clinical care will flourish. For the ICU clinical governance requires the culture, the systems and the support mechanisms to achieve good clinical performance and ensuring that quality improvement is embedded into the unit's routine. This includes action to ensure risks are managed, adverse effects are rapidly detected, openly investigated and lessons learned, good practice is rapidly disseminated and systems are in place to ensure continuous improvements in clinical care. There must be systems to ensure all clinicians have the right education, training, skills and competencies to deliver the care needed by patients. There must be systems in place to recognise and act on poor performance.

Essential components of clinical governance

Clear management arrangements

Eveyone must know who they are accountable to, the limits of their decision making and who must be informed in the decision making process.

Quality improvement

Through the process of clinical audit the standard of practice is monitored and changes effected to improve quality.

Clinical effectiveness

Evidence based practice is essential where evidence exists to support clinical decisions. Protocols and guidelines standardise practice.

Risk assessment and management

A register of clinical risks should be kept, to which new risks are appended as they are assessed. An action plan should be developed for managing each risk.

Staff and organisational development

Including continued professional education, clinical supervision and professional regulation.

Patient input

Complaints monitoring should be used to learn lessons and improve practice within ICU. Patient and relative surveys can be used to adapt quality initiatives to the needs of patients.

See also:

Audit, p570

Audit

Audit has become an essential part of medical practice. The main purpose is to improve quality of care which, in the intensive care unit, must involve all members of the multidisciplinary team. Change in practice in one discipline will inevitably have a knock-on effect in others. Audit may involve a review of activity, performance against predetermined indicators or cost-effectiveness. Audit may focus on specific topics or may encompass the performance of several intensive care units. Successful audit requires commitment from senior staff to ensure practice is defined, data are collected and change is effected where necessary. Where change is suggested by audit a further review is required to ensure that such change has occurred.

Data collection

Ideally, a basic data set should be common to all intensive care units nationally to allow meaningful comparisons to be made. This requires the data set to be detailed enough to answer questions posed but not so detailed that collection becomes unsustainable. Resources must be provided in terms of computer databases and staff to collect and analyse data. Those collecting the data should be provided with regular summary reviews to ensure that enthusiasm continues, and quality control is maintained. Methods of data entry should consider the time involved and the fact that most of those collecting data are not keyboard experts. Typographical mistakes destroy the value of collected data such that error trapping and data validation must form part of the housekeeping in any database used. Some audit topics require data collection that is not part of the basic data set. Collecting appropriate data requires clarity in setting the question to be answered and care in choosing data items that will truly answer the question.

Audit meetings

Regular audit meetings should follow a predefined timetable. This helps to ensure maximum staff attendance and also sets target dates for data collection and analysis. Audit meetings should be chaired and have defined aims. Discussion of the topic being audited must lead to recommended changes in practice and these must be followed through after the meeting. It is clear that all staff cannot attend all meetings. Dissemination of information prior to implementing proposed changes is necessary to stand some chance of carrying them through.

See also:

Clinical governance, p568

ICU scoring systems

Various ICU scoring systems have evolved to provide:

- An index of disease severity, e.g. APACHE, SAPS.
- An index of workload and consumption of resources, e.g. TISS.
- A means of comparison for
- (i) Auditing performance—either in the same ICU or between ICUs.
- (ii) Research, e.g. evaluation of new products or treatment regimens.
- Patient management objectives, e.g. sedation, pressure area care.

Other than the Glasgow Coma Score, there is no universal system practised by every ICU. While APACHE is the predominant system used in the USA and UK for scoring disease severity, SAPS is more popular in mainland Europe. Interpretation of the same system can also be highly variable.

TISS (Therapeutic Intervention Scoring System)

- This system attaches a score to procedures and techniques performed on an individual patient (e.g. use and number of vasoactive drug infusions, renal replacement therapy, administration of enteral nutrition).
- It has been used by some ICUs to develop a means of costing individual patients by attaching a monetary value to each TISS point scored.
- It is also used as an index of workload activity.
- A discharge TISS score can be used to estimate the amount of nursing interventions required for a patient in step-down facilities (e.g. a high dependency unit) or on the general ward.

- TISS does not accurately measure nursing workload activity as it fails to cater for tasks and duties such as coping with the irritable or confused patient, dealing with grieving relatives, etc.

Glasgow Coma Scale

First described by Teasdale and Jennett in 1974, it utilises eye opening, best motor response and best verbal response to categorise neurological status. It is the only system used universally in ICUs, though limitations exist in mechanically ventilated, sedated patients. It can be used for prognostication and is also frequently used for therapeutic decision making, e.g. elective ventilation in patients presenting with a GCS <8.

Sedation

A variety of systems gauge and record the level of sedation in a mechanically ventilated patient. This assists the staff to titrate the dose of sedative agents to avoid either over- or under-sedation. The forerunner developed in 1974 was the Ramsay Sedation Score which consists of a 6-point scoring system separated into 3 awake and 3 asleep levels where the patient responds to a tap or loud auditory stimulus with either brisk, sluggish or no response at all. The main problem lies in achieving reproducibility of the tap or loud auditory stimulus. We currently use an 8-point system developed in-house.

Glasgow Coma Scale

Score	Eyes open	Best motor response	Best verbal response
6	—	obeys commands	—
5	—	localises pain	orientated
4	spontaneously	flexion withdrawal	confused
3	to speech	decerebrate flexion	inappropriate words
2	to pain	decerebrate extension	incomprehensible sounds
1	never	no response	silent

UCLH Sedation Score

3	Agitated and restless
2	Awake and uncomfortable
1	Aware but calm
0	Roused by voice, remains calm
-1	Roused by movement
-2	Roused by noxious or painful stimuli
-3	Unrousable
A	Natural sleep

ICU scoring systems—APACHE II

APACHE (Acute Physiology And Chronic Health Evaluation)

- Devised by Knaus et al, this system utilises a point score derived from the degree of abnormality of readily obtainable physiological and laboratory variables in the first 24h of ICU admission, plus extra points for age and chronic ill health.

- The summated score provides a measure of severity while the percentage risk of subsequent death can be computed from specific coefficients applied to a wide range of admission disorders (excluding burns and cardiac surgery).

- APACHE I, first described in 1981, utilised 34 physiological and biochemical variables.

- A simplified version (APACHE II) utilising just 12 variables was published in 1985 and extensively validated in a number of countries.

- A further refinement published in 1990, APACHE III, claims to improve upon the statistical predictive power by adding five new physiological variables (albumin, bilirubin, glucose, urea, urine output).

- Changing thresholds and weighting of existing variables.

- Comparing both admission and 24h scores.

- Incorporating the admission source (e.g. ward, operating theatre).

- Reassessing effects of age, chronic health and specific disease category. Wide acceptance of APACHE III may be limited as its risk stratification system is proprietary and has to be purchased.

Key paper

Knaus WA, et al. APACHE II: a severity of disease classification system. Crit Care Med 1985; 13:818–29

Acute physiology score

	+4	+3	+2	+1	0	+1	+2	
Core temperature (°C)	≥41	39–40.9		38.2–38.9	36–38.4	34–35.9	32–33.9	3
Mean BP (mmHg)	≥160	130–159	110–129		70–109		50–69	
Heart rate (/min)	≥180	140–179	110–139		70–109		55–69	4
Respiratory rate (/min)	≥50	35–49		25–34	12–24	10–11	6–9	
If $FIO_2 ≥ 0.5$: A-aDO_2 (mmHg)	≥500	350–499	200–349	<200				
If $FIO_2 < 0.5$: PO_2 (mmHg)				>70		61–70		5
Arterial pH	≥7.7	7.6–7.69		7.5–7.59	7.33–7.49		7.25–7.32	7
Serum Na^+ (mmol/l)	≥180	160–179	155–159	150–154	130–149		120–129	1
Serum K^+ (mmol/l)	≥7	6–6.9		5.5–5.9	3.5–5.4	3–3.4	2.5–2.9	
Serum creatinine (µmol/l) NB double points score if acute renal failure								
	≥300	171–299	121–170		50–120		<50	
Haematocrit (%)	≥60		50–59.9	46–49.9	30–45.9		20–29.9	
Leukocytes (/mm^3)	≥40		20–39.9	15–19.9	3–14.9		1–2.9	
Neurological points= 15 - Glasgow coma score								

Age points:

Years	≤44	45–54	55–64	65–74	≥75
Points	0	2	3	5	6

Chronic health points

2 points for elective post-operative admission or 5 points if emergency operation or non-operative admission, if patient has either:

- Biopsy proven cirrhosis, portal hypertension or previous hepatic failure
- Chronic heart failure (NYHA Grade 4),
- Chronic hypoxia, hypercapnia, severe exercise limitation, 2° polycythaemia or pulmonary hypertension
- Dialysis-dependent renal disease
- Immunosuppression by disease or drugs

ICU scoring systems—SAPS II

- Has a similar role to APACHE II, but more widely utilised in mainland Europe, the Simplified Acute Physiology Score (SAPS) was devised by LeGall et al in 1984 (SAPS I) and modified by the same group in 1993 (SAPS II). A SAPS III score is in development.
- As for APACHE II, burns and cardiac surgical patients are excluded from analysis.
- The original version used 14 readily measured clinical and biochemical variables while the updated version, SAPS II, comprises 12 physiology variables, age, type of admission (medical, scheduled or unscheduled surgical) and three underlying disease variables.
- A point score is based on the degree and prognostic importance of derangement of these variables in the first 24h following ICU admission. The point scoring was assigned following logistic regression modelling of data obtained from 8369 patients in 137 adult ICUs in both Europe and North America and validated in a further 4628 patients.
- The claimed advantage of this system is that it estimates the risk of death without having to specify a primary diagnosis.

Key paper

Le Gall JR, et al. A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. JAMA 1993;270: 2957–63

Point score in brackets	
Age	<40 (0); 40–59 (7); 60–69 (12); 70–74 (15); 75–79 (16); ≥80 (18)
Heart rate (bpm)	<40 (11); 40–69 (2); 70–119 (0); 120–159 (4); ≥160 (7)
Systolic BP (mmHg)	<70 (13); 70–99 (5); 100–199 (0); ≥200 (2)
Body temp (°C)	<39 (0); ≥39 (3)
PaO_2/FIO_2 (kPa) only if ventilated or on CPAP	<13.3 (11); 13.3–26.5 (9); ≥26.6 (6)
Urine output (l/day)	<0.5 (11); 0.5–0.999 (4); ≥1 (0)
Serum urea (mmol/l)	<10 (0); 10–29.9 (6); ≥30 (10)
White cell count (/mm^3)	<1 (12); 1–19.9 (0); ≥20 (3)
Serum K^+ (mmol/l)	<3 (3); 3–4.9 (0); ≥5 (3)
Serum Na^+ (mmol/l)	<125 (5); 125–144 (0); ≥145 (1)
Serum $HCO3^-$ (mmol/l)	<15 (6); 15–19 (3); ≥20 (0)
Serum bilirubin (µmol/l)	<68.4 (0); 68.4–102.5 (4); ≥102.6 (9)
Glasgow Coma Score	<6 (26); 6–8 (13); 9–10 (7); 11–13 (5); 14–15 (0)
Chronic disease	metastatic cancer (9), haematological malignancy (10), AIDS (17)
Type of admission	scheduled surgical (0); medical (6); unscheduledsurgical (8)

ICU scoring systems—SOFA

A limitation of the APACHE and SAPS scoring systems is that they were designed and validated on data obtained during the first 24 hours of intensive care admission. Various systems have been developed to enable daily scoring (e.g. Sequential Organ Failure Assessment (SOFA), Riyadh Intensive Care Program (RIP) score, Multiple Organ Dysfunction Score, etc.) to allow a better assessment of change in the patient's condition.

As the physiological and biochemical status of the patient is determined in part by the disease severity, but also by the degree of medical intervention, these sequential scoring systems incorporate the use of various therapies and procedures.

The SOFA system was initially designed to improve patient characterisation for multicentre drug trials in sepsis (SOFA initially stood for Sepsis Organ Failure Assessment) but has subsequently been applied to intensive care patients in general, with 'Sequential' being substituted for 'Sepsis'.

Although it has not been validated in the sense that a point score denoting severity of dysfunction in one organ system does not translate directly to an equivalent severity in another organ, it has been used successfully to prognosticate and to follow changes in patient status throughout their intensive care stay.

Point score in brackets

	0	1	2	3	4
Respiratory PaO$_2$:FIO$_2$ ratio (mmHg)	>400	≤400	≤300	≤200*	<100*
Renal Creatinine (mg/dl) or Urine output (ml/d)	<1.2	1.2–1.9	2.0–3.4	3.5–4.9 or <500ml/d	≥5.0 or <200ml/d
Hepatic Bilirubin (mg/dl)	<1.2	1.2–1.9	2.0–5.9	6.0–11.9	≥12.0
Cardiovascular Mean arterial pressure (mmHg)	No hypo-tension	MAP >70	Dopamine≤5 or dobutamine (any dose)†	Dopamine>5 or epinephrine≤0.1 epinephrine≤0.1†	Dopamine>15 or epinephrine>0.1 epinephrine>0.1†
Haematological Platelet count($\times$10^3/mm^3)	>150	≤150	≤100	≤50	≤20
Neurological Glasgow Coma Score	15	13–14	10–12	6–9	<6
*With ventilatory support					
†Adrenergic agents administered for at least 1 h (doses in µg/kg/min)					

Conversion factors:

- PaO$_2$:FIO$_2$ to KPa: divide by 7.5
- Creatinine to µmol/l: multiply by 88
- Bilirubin to µmol/l: multiply by 17.1

Key paper

Moreno R, Vincent JL, Matos R, et al. The use of maximum SOFA score to quantify organ dysfunction/failure in intensive care. Results of a prospective, multicentre study. Working Group on Sepsis related Problems of the ESICM. Intensive Care Med 1999; 25:686-96

ICU scoring systems—trauma

Scoring systems have been developed in trauma for:

- Rapid field triage to direct the patient to appropriate levels of care
- Quality assurance
- Developing and improving trauma care systems by categorising patients and identifying problems within the systems
- Making comparisons between groups from different hospitals, in the same hospital over time, and/or undergoing different treatments

The Injury Severity Score (ISS) is a severity scoring system patients based on the anatomical injuries sustained. The Revised Trauma Score (RTS) utilises measures of physiological abnormality to predict survival. A combination of ISS and RTS—TRISS—was developed to overcome the shortcomings of anatomical or physiological scoring alone. The TRISS methodology uses ISS, RTS, patient age and whether the injury was blunt or penetrating to provide a measure of the probability of survival.

Injury Severity Score

1. Use AIS90 (Abbreviated Injury Score 1990) dictionary to score injury

2. Identify highest abbreviated injury scale score for each of the following:

- Head and neck
- Abdomen and pelvic contents
- Bony pelvis and limbs
- Face
- Chest
- Body surface

3. Add together the squares of the three highest area scores.

Revised trauma score

	Measure	Coded value	x = Score weighting
Respiratory rate (breaths/min)	10–29	4	
	>29	3	
	6–9	2	0.2908
	1–5	1	
	0	0	
Systolic blood pressure (mmHg)	>89	4	
	76–89	3	
	50–75	2	0.7326
	1–49	1	
	0	0	
Glasgow Coma Score	13–15	4	
	9–12	3	
	6–8	2	0.9368
	4–5	1	
	3	0	
		Total = revised trauma score	