Aims of obstetric critical care management

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The aims of critical care management are broad. Critical illness in pregnancy is especially pertinent as the patient is usually young and previously fit, and management decisions must also consider the fetus. Assessment must consider the normal physiological changes of pregnancy, which may complicate diagnosis of disease and scoring levels of severity. Pregnant women may present with any medical or surgical problem, as well as specific pathologies unique to pregnancy that may be life threatening, including pre-eclampsia and hypertension, thromboembolic disease and massive obstetric haemorrhage. There are also increasing numbers of pregnancies in those with high-risk medical conditions such as cardiac disease. As numbers are small and clinical trials in pregnancy are not practical, management in most cases relies on general intensive care principles extrapolated from the non-pregnant population. This chapter will outline the aims of management in an organ-system-based approach, focusing on important general principles of critical care management with considerations for the pregnant and puerperal patient.

Key words: pregnancy; high risk; complications; pre-eclampsia; postpartum haemorrhage; thromboembolism; intensive care; critical care.

GENERAL OVERVIEW

Maternal mortality is fortunately rare in the UK, with 13.95 maternal deaths per 100,000 deliveries in 2003–2005.¹ However, despite modern-day advances in care,
this figure has remained static over the last few decades, and this may relate to a higher number of high-risk pregnancies progressing to term. Worldwide, maternal mortality is greater with 55–920 maternal deaths per 100 000 live births, with the highest rates in sub-Saharan Africa. The most common reasons for intensive care unit (ICU) admissions in the UK are pre-eclampsia, sepsis and haemorrhage. Overall, 0.9% of pregnant women require ICU admission in the UK, comparable to US figures. The most common cause of maternal death on ICU is acute respiratory distress syndrome (ARDS). UK maternal mortality could be improved with prompt recognition of critical illness, earlier use of critical care facilities and earlier senior involvement. Perinatal mortality rates are up to 20–25% depending on the underlying maternal diagnosis.

The assessment and management of obstetric admissions to critical care can be challenging, with unique disease states and physiological changes seen. These changes occur in all major systems and persist for up to 6 weeks post partum. In 50–80% of cases, pregnant women require ICU admission due to a direct obstetric cause; the remainder relate to medical causes. There may be diseases specific to pregnancy (massive obstetric haemorrhage, amniotic fluid embolism, pre-eclampsia, peripartum cardiomyopathy); an increased susceptibility to certain diseases due to pregnancy (venous thromboembolism, urinary tract infection, varicella pneumonia); pre-existing disease exacerbation (asthma, cardiac disease); or incidental diseases during pregnancy (e.g. diabetic ketoacidosis). The requirement for critical care support for one or more organ failures usually results from the development of a multisystem disorder such as shock, ARDS or sepsis.

The aim of critical care management in any population is to ensure adequate oxygen delivery and tissue perfusion. There are specific conditions requiring attention in pregnancy, and this review will consider general ICU principles and these with reference to obstetric physiology. The altered maternal physiology should be considered during each stage of assessment, resuscitation, monitoring, use of pharmacological therapies, and single or multiple organ support. Young, previously healthy patients often show relative compensation in critical illness. The signs of sepsis and haemorrhage are often masked initially and abnormal signs may overlap normal signs of pregnancy. Some signs always indicate abnormality, including tachypnoea and metabolic acidosis. Obstetric and medical staff should be trained in the recognition of critical illness in this population as the disease processes can follow a rapid and fulminant course.

The effects on fetal perfusion are dependent on placental perfusion and oxygen delivery, both reflecting maternal wellbeing. The fetus is adapted to living in a relatively hypoxic environment with the oxygen dissociation curve shifted to the left, high haematocrit and high cardiac output (CO). Despite this, small changes in maternal homeostasis may have an adverse effect on the fetus. If the mother does become critically ill, premature delivery may be indicated with the associated neonatal complications of respiratory distress syndrome, jaundice, intracranial haemorrhage and necrotizing enterocolitis.

AIMS OF ORGAN SUPPORT IN CRITICAL CARE

General supportive care

Immediate resuscitation is the primary aim in the management of any critically ill patient, with systematic assessment of deranged physiology using an organ-based systematic approach. This is generic, irrespective of the underlying pathology, and is followed by more specific diagnostic consideration when the patient is more stable.
Appropriate investigations and procedures are then carried out, depending on the clinical history and examination. It is important not to withhold or delay useful investigations because the patient is pregnant.

The gestational age and condition of the fetus must always be considered, as well as the effects of any drugs or procedures on the fetus. The obstetric team should perform a fetal scan to assess viability. Often if the mother is or has been critically ill, the fetus may have succumbed. Once this is established, liaison with obstetricians to deliver the baby will usually improve maternal physiology, although delivery itself is associated with significant temporary haemodynamic demands and changes. If the fetus is viable, the advisability of delivery needs a multidisciplinary discussion balancing the fetal risks of prematurity versus any maternal benefits from delivery. The mother's health should be the priority. The fetus is at significant risk if the mother is seriously ill, particularly if she is acidic, and regular fetal monitoring is appropriate.

Fetal management primarily involves maternal resuscitation, maintaining adequate placental oxygenation and perfusion. Delivery may be indicated in some settings of severe maternal illness such as cardiac arrest, severe asthma, acute fatty liver of pregnancy or pre-eclampsia, or with fetal distress. When considering the timing of delivery, the effects of drugs on fetal physiology and the requirement for neonatal resuscitation should be considered. Drugs are classed according to the risk of fetal effects into Category A (no fetal risk) to Category D (fetal risk), and Category X (contra-indicated). The maternal volume of distribution is increased and glomerular filtration rate (GFR) is elevated in pregnancy, so higher doses are needed for drugs with renal elimination. Sedative effects on fetal respiratory function should be anticipated, although polarized agents such as neuromuscular blocking agents do not cross the placenta.

Critical care involves intensive monitoring and physiological support for patients with life-threatening but potentially reversible conditions. Patients should be managed in either an ICU (Level 3) or high-dependency (Level 2) setting. Level 3 usually involves patients with multi-organ failure and/or requiring mechanical ventilation, while Level 2 involves non-invasive ventilation (NIV), renal replacement therapy or intensive monitoring.

Early involvement and planning should involve all members of the multidisciplinary team. This includes obstetricians, midwives, physicians (obstetric physicians if available), intensivists, anaesthetists, haematologists, paediatricians and neonatologists. Elective ICU beds should be booked for certain patients such as those with significant cardiac disease undergoing elective caesarean section.

Early recognition of critical illness is essential. There is good evidence that early intervention in the first 6 h of severe sepsis influences survival. Ideally, early warning scoring systems adapted to pregnancy physiology should be implemented on obstetric wards to identify patients at an early stage. ICU care can often be commenced in the operating theatre or emergency department (ED) prior to transfer to the ICU to avoid delays, and stabilization and elective intubation may be necessary prior to transfer.

Aims should also include adherence to recent developments in critical care practice including the Surviving Sepsis Campaign guidelines, considered use of activated protein C, insulin therapy to maintain normoglycaemia, corticosteroids in septic shock, lung protective ventilatory strategies in ARDS management, and early goal-directed therapy for severe sepsis and septic shock. Although not written with the obstetric patient in mind, most aspects of management should not differ dramatically.
Haemodynamic management

The aims of cardiovascular support in any setting are to maintain adequate cardiac output (CO) and blood pressure (BP). There is a 20% increase in maternal oxygen demand in pregnancy; CO increases by 30–50% due to an increase in stroke volume and heart rate, and BP is reduced by 5–10 mm Hg by mid-pregnancy. There is no change in central venous pressure (CVP) or pulmonary artery wedge pressure (PAWP) as systemic and pulmonary vascular resistance are both reduced. These haemodynamic changes begin as early as 8 weeks, and gradually return to normal 2–12 weeks post partum.11

The supine hypotension syndrome is an important consideration after 24 weeks. It relates to compression of the inferior vena cava by the gravid uterus, and can lead to a dramatic drop in preload, leading to a 25–30% drop in CO, severe hypotension and bradycardia. It can be reduced by positioning in a lateral tilt although a full left lateral position is sometimes required.

The most significant cardiovascular challenge occurs at birth. Up to 500 mL of blood is autotransfused back into the circulation following relief of aortocaval compression by the fetoplacental unit and contraction of the uterus, and CO may increase by up to 80% of preterm baseline. These fluid shifts are especially challenging in parturients with cardiac disease, who should be monitored for 72 h post partum.13

Shock

Cardiovascular support may be required in states of circulatory shock. In shock, reduced tissue oxygenation leads to anaerobic metabolism, reflected by an increased serum lactate and reduced maternal central venous oxygen saturations (SvO₂). This will affect fetal oxygenation despite adaptation to a relatively hypoxic environment.

Lactate levels >2 mmol/L indicate tissue hypoxia except in settings with poor lactate clearance such as liver failure. Serial measurements are useful, for example, in septic shock (Table 1).14

The most common causes of shock in the obstetric population are major haemorrhage and sepsis. When reversible causes have been controlled, support of the

<table>
<thead>
<tr>
<th>Type of shock</th>
<th>Pathophysiology</th>
<th>Cardiac output</th>
<th>Systematic vascular resistance</th>
<th>Examples of causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypovolaemia</td>
<td>Loss of circulating volume</td>
<td>Low</td>
<td>High</td>
<td>Massive haemorrhage, diabetic ketoacidosis, burns</td>
</tr>
<tr>
<td>Distributive</td>
<td>Pathological vasodilatation</td>
<td>High/low</td>
<td>Low</td>
<td>Sepsis, liver failure, pancreatitis, anaphylaxis</td>
</tr>
<tr>
<td>Cardiogenic</td>
<td>Severe pump failure</td>
<td>Low</td>
<td>High</td>
<td>Cardiomyopathy, valvular dysfunction</td>
</tr>
<tr>
<td>Obstructive</td>
<td>Obstruction to cardiac output</td>
<td>Low</td>
<td>High</td>
<td>Pulmonary embolism, amniotic fluid embolus, tamponade</td>
</tr>
<tr>
<td>Neurogenic</td>
<td>Loss of sympathetic outflow if lesion above T6</td>
<td>Low</td>
<td>Low</td>
<td>Spinal trauma, intracranial haemorrhage</td>
</tr>
</tbody>
</table>

Table 1. Types of shock.
cardiovascular system may involve fluid administration, correction of heart rate and rhythm disorders, the use of vasoactive agents, thrombolysis, pacemakers, ventilatory support and mechanical devices. Invasive or non-invasive haemodynamic monitoring is an important tool. Techniques may be invasive (lithium dilution pulsed contour analysis and the pulmonary artery catheter), semi-invasive (oesophageal Doppler) or non-invasive (echocardiography).

Fluids

Fluid administration is an important part of most resuscitation scenarios, aiming to improve microvascular blood flow by increasing plasma volume, and improve CO by the Frank-Starling mechanism. However, the use of fluids in obstetrics should be more cautious than in the non-obstetric setting. Even in a normal pregnancy, colloid oncotic pressure (COP) is reduced by 14% (from 20.8 to 18 mm Hg). This reduction in COP, when combined with any condition predisposing to either increased capillary leak (e.g. in pre-eclampsia and many critical illness states) or raised left atrial pressure, can relatively easily lead to pulmonary oedema. It is not thought to be as common as this suggests, because pulmonary lymphatic drainage is increased in pregnancy.

The choice of fluid used will depend on the setting. In major haemorrhage, replacement is needed with blood products. Otherwise, the choice between crystalloid and colloid remains under debate. Excessive use of normal saline leads to hyperchloraemic acidosis, and Hartmann’s solution is currently the most ‘physiological’ crystalloid in use. Colloids remain in the intravascular compartment for longer. Overall, the choice will depend on the underlying diagnosis, local availability, the evaluation of the content of each fluid type, and the benefits and complications of each (see Table 2). The concept of a fluid challenge requires haemodynamic monitoring to assess volume responsiveness to a set volume of fluid. Following this, a 20% rise in stroke volume suggests intravascular depletion, and sufficient intravascular volume is suggested when the rise is sustained. Small rises or a fall in the stroke volume suggest fluid overload as the myocardium is stretched ‘over the Starling curve’. Obstetric patients are best managed with a neutral or even negative fluid balance, as the development of acute prerenal failure is usually reversible if recognised and treated early, compared with the potential risks of non-cardiogenic pulmonary oedema or ARDS.

<table>
<thead>
<tr>
<th>Fluid</th>
<th>Ionic content (mmol/L)</th>
<th>pH</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal saline (NaCl 0.9%)</td>
<td>Na$^+$ 154, Cl$^-$ 154</td>
<td>5.0</td>
<td>Hyperchloraemic acidosis</td>
</tr>
<tr>
<td>5% dextrose</td>
<td>Nil</td>
<td>4.0</td>
<td>Hyponatraemia, oedema</td>
</tr>
<tr>
<td>Hartmann’s</td>
<td>Na$^+$ 131, K$^+$ 5, Cl$^-$ 111, Ca$^{2+}$ 2, HCO$_3^-$ 29</td>
<td>6.5</td>
<td>Fluid overload (with all fluids), K$^+$ may accumulate</td>
</tr>
<tr>
<td>Gelofusin</td>
<td>Na$^+$ 154, K$^+$ 0.4, Cl$^-$ 154, Ca$^{2+}$ 0.4</td>
<td>7.4</td>
<td>Allergy (&lt;0.1%), hyperchloraemia</td>
</tr>
<tr>
<td>Albumin 4.5%</td>
<td>Na$^+$ 150, K$^+$ 2, Cl$^-$ 120</td>
<td>7.4</td>
<td>Transfusion reactions, TRALI</td>
</tr>
</tbody>
</table>

TRALI, transfusion-related lung injury.
Furthermore, the appropriate management of oliguria in these patients is not necessarily a fluid challenge, as discussed further in the renal section.

Cardiac failure

Cardiac failure may be primarily left sided with pulmonary oedema, right sided with evidence of hepatic and renal congestion, or biventricular. Reversible causes such as coronary ischaemia or pulmonary embolism should be managed as appropriate. Non-invasive continuous positive airways pressure (CPAP) is a very effective treatment for cardiogenic pulmonary oedema, and will increase CO, reduce left ventricular afterload, increase functional residual capacity (FRC) and respiratory mechanics, and reduce work of breathing. Invasive ventilation may be needed if the woman is severely acidotic, hypercapnic, hypotensive or has very poor left ventricular function. Vasodilator therapy is important, and both glyceryl trinitrate (GTN) and hydralazine are safe in pregnancy. Loop diuretics are used to reduce pulmonary congestion, although they may reduce CO and uteroplacental perfusion if hypovolaemic. If inotropes are needed, dobutamine is safe in pregnancy. Newer inotropes such as levosimendan may improve arterioventricular coupling, although there are only case reports of use in pregnancy in peripartum cardiomyopathy. Mechanical devices to augment CO such as ventricular assist devices and intra-aortic balloon pumps may be required.

Vasoactive agents

Heart rate and rhythm disorders are corrected in the usual way according to resuscitation council guidelines. Most supraventricular tachycardias and ventricular ectopics require no drug therapy in pregnancy, and vagal manoeuvres such as carotid sinus massage should be tried first in paroxysmal supraventricular tachycardia. Atrial fibrillation should be restored to sinus rhythm in pregnancy with electrical cardioversion, or rate controlled with digoxin or cardioselective beta-blockers. Replacement of potassium and magnesium may be required, then chemical or electrical cardioversion as appropriate, or use of specific anti-arrhythmic agents. Cardioselective beta-blockers, diltiazem, verapamil and adenosine are safe; however, amiodarone should be avoided as it can inhibit fetal thyroid function. Vasopressors are often used for hypotension in the setting of obstetric regional anaesthesia. Ephedrine may lead to maternal tachycardia due to its chronotropic effects on the cardiac beta-1 receptor and reduced fetal pH, although it is less likely to cause uteroplacental vasoconstriction. Phentolamine, an alpha-1 adrenergic agonist and powerful arteriolar constrictor, causes less fetal acidosis although it may reduce maternal heart rate and therefore CO. If inotropes or more powerful vasoressors are required in an ICU setting, the effects on uteroplacental perfusion should be considered, and CO monitoring is useful. The choice of agent will depend on the mean arterial pressure (MAP), CO and systematic vascular resistance (SVR), and should follow appropriate fluid resuscitation. In the setting of vasodilatory shock with low SVR and high CO (sepsis, liver failure), sympathomimetic vasoressors such as norepinephrine are used. Vasopressin has been used in some settings such as resistant septic shock and cardiac arrest, but reduced blood flow to some organs may occur so it should be reserved for ‘salvage’ therapy. In cardiogenic shock, increased inotropy from beta-1 agonism may be useful using dobutamine (and epinephrine with added vasoconstrictive effects). Inodilators are useful when low CO occurs with vasoconstriction (high SVR), with agents including milrinone and the calcium-sensitizer levosimendan (Table 3).
Hypertension complicates 12% of pregnancies and may be classified into pre-eclampsia, gestational hypertension, chronic essential hypertension and malignant hypertension presenting in pregnancy. The overall management strategy of pre-eclampsia with delivery as a prime goal is discussed in detail elsewhere. There is no single ideal anti-hypertensive regime used for acute severe hypertension in pregnancy, and most units have their own protocol. Intravenous hydralazine and labetalol are equally effective but labetalol is preferred as it has fewer side effects. Sodium nitroprusside is an effective vasodilator, and is therefore a good choice if pulmonary oedema is present, and its short half-life is useful when titrating the dose. However, toxicity may occur with cyanide or thiocyanate accumulation, usually in those with renal failure and if treated for more than 24 h. GTN is useful and safe for short-term use, although mainly as a venodilator as it has little effectiveness in hypertensive emergencies and so is not usually a first-line agent, and problems result with tachyphylaxis. Oral nifedipine, doxasocin and alpha-methyldopa are oral options. Angiotensin-converting enzyme inhibitors are teratogenic and are therefore contra-indicated, although they may be life-saving in some cases of malignant hypertension including scleroderma.

Respiratory management

The overall aim of respiratory management is to maintain gas exchange. This encompasses airway management, administering oxygen therapy and ensuring adequate
ventilation (CO\textsubscript{2} clearance). These general principles are as for the non-pregnant population, with added considerations of the physiological changes, including the left lateral tilt in positioning, and the need in later pregnancy to consider a delivery plan. It is important to remember that oxygen delivery to the tissues and effective CO\textsubscript{2} removal involves the heart and circulation as well as the lungs. Oxygen delivery to the tissues involves a cascade of processes depending on alveolar oxygen concentration, oxygen transfer, haemoglobin and the oxygen dissociation curve, then diffusion from capillary blood into mitochondria along a concentration gradient. Defects can occur at any of these levels.

The differential diagnosis of primary respiratory failure in pregnancy is broad, and the changes in respiratory physiology should be remembered in assessment and management. Erect partial pressure of oxygen (PaO\textsubscript{2}) increases by the end of the first trimester, and falls during each of the following trimesters. This is due to an increased arteriovenous oxygen difference as oxygen consumption increases above CO with the advancement of pregnancy. After mid-gestation, PaO\textsubscript{2} is <13.1 kPa in supine patients due to airway closing capacity being above FRC, and also from aortocaval compression. The reduced FRC and greater oxygen consumption make episodes of desaturation more rapid. Adequate fetal oxygenation requires a maternal PaO\textsubscript{2} > 9.2 kPa, corresponding to a maternal arterial oxygen saturations (SaO\textsubscript{2}) > 95%\textsuperscript{34}, much higher than the saturations usually tolerated outside pregnancy.

It is important to consider the normal progressive respiratory alkalosis when considering respiratory management, as ventilation requirements may change depending on the stage of pregnancy. In severe asthma, a ‘normal’ partial pressure of CO\textsubscript{2} (pCO\textsubscript{2}) of 4–5.5 kPa is usually a warning of impending respiratory failure. In pregnancy, this is, in fact, relative hypercapnia as the usual upper limit in pregnancy is 3.5 kPa. The effects of pCO\textsubscript{2} on fetal wellbeing are not clear, although they are likely to be detrimental with acidosis leading to reduced ability of fetal haemoglobin to bind oxygen. A diffusion gradient of approximately 1.3 kPa is needed for placental pCO\textsubscript{2} clearance\textsuperscript{35}, and high maternal levels may interfere with this. A maternal pCO\textsubscript{2} target of <5.9 kPa or pH > 7.30 has therefore been suggested\textsuperscript{36}, avoiding hypercapnia (Table 4).

**Upper airway**

Airway management may be challenging in obstetric practice. There are changes in maternal anatomy with increased upper airway oedema, especially in pre-eclampsia where fluid retention enlarges the tongue and makes identification of airway landmarks more

<table>
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<tr>
<th>Table 4. Causes of respiratory failure in pregnancy.</th>
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<tbody>
<tr>
<td><strong>Pulmonary causes</strong></td>
</tr>
<tr>
<td>Asthma, severe pneumonia, pleural effusion, pneumothorax, pulmonary haemorrhage, interstitial lung disease, exacerbation of underlying respiratory disease (e.g. cystic fibrosis, chronic obstructive pulmonary disease, bronchiectasis, pulmonary hypertension), atypical infection (including human immunodeficiency virus), respiratory muscle myopathies (hypercapnic respiratory failure)</td>
</tr>
<tr>
<td>Acute respiratory distress syndrome (ARDS) and acute lung injury (see later)</td>
</tr>
<tr>
<td><strong>Cardiac causes</strong></td>
</tr>
<tr>
<td>Cardiogenic pulmonary oedema, e.g. peripartum cardiomyopathy, mitral stenosis</td>
</tr>
<tr>
<td>Iatrogenic fluid overload</td>
</tr>
<tr>
<td>Tocolytic pulmonary oedema (rare now with alternatives to beta-sympathomimetics)</td>
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</tbody>
</table>
difficult. Any neck or face oedema in a woman with pre-eclampsia should forewarn of a likely difficult intubation. These patients may even develop stridor and may have difficult extubations. Airway oedema in pre-eclampsia can even lead to obstructive sleep apnoea. Sleep-disordered breathing is probably underdiagnosed in pregnancy and may have adverse fetal effects. Obesity is more common and correlates with difficult intubations, instrumental deliveries, a higher incidence of postpartum haemorrhage, and an even greater incidence of gastric acid aspiration during general anaesthesia. The upper airway in pregnancy is prone to contact bleeding with any airway manipulation. This mucosal swelling leads to a smaller laryngeal inlet. Any airway intervention should involve a skilled anaesthetist with a fluent difficult/failed intubation drill.

Ventilation

The aims of ventilation are to oxygenate, ventilate and relieve the work of breathing. In pregnancy, ventilation can be problematic. As in the non-pregnant patient, ventilation may be invasive, through an endotracheal tube or tracheotomy, or non-invasive, through a tightly fitting facemask. NIV may exert CPAP or bi-level positive airway pressure (BiPAP). CPAP is the application of a constant positive end-expiratory pressure, called ‘positive end-expiratory pressure’ in the invasively ventilated patient. Non-invasive CPAP differs from BiPAP in several ways. BiPAP enables spontaneous breathing over two pressure levels, and is therefore more effective at clearing CO₂, hence its use in hypercapnic respiratory failure. CPAP circuits can deliver a higher fractional inspired oxygen concentration (FiO₂) and can be humidified, and the FiO₂ can be measured accurately. With BiPAP, FiO₂ is not measured accurately, oxygen is entrained in L/min, the circuit tolerates leaks, and the delivered FiO₂ is dependent on the inspiratory flow rate.

Non-invasive ventilation. The evidence for acute NIV is well established in the treatment of hypercapnic respiratory failure in chronic obstructive pulmonary disease, where it reduces the need for intubation in mildly acidotic patients. There is also good evidence for NIV in cardiogenic pulmonary oedema and in immunocompromised states. It has physiological benefit in other causes of respiratory failure, but should be used in a controlled, monitored setting as a trial of therapy. Patients should be awake with good respiratory drive, haemodynamically stable and without excessive respiratory secretions. Those with more marked acidosis (pH < 7.25) should be considered for earlier invasive ventilation. There is less evidence for its use in other causes of hypoxaemic respiratory failure, but it has been used in asthma, pneumonia, ARDS and others including postoperative cases. There is little evidence for its use in the obstetric population, although it has been used in sleep-disordered breathing during pregnancy. NIV cannot therefore be currently recommended except as a closely monitored trial of therapy in selected obstetric patients, in an ICU setting. Furthermore, there is a theoretical even greater risk of gastric acid aspiration with the gastric distention that occurs with NIV.

Invasive ventilation. Invasive ventilatory support may be necessary in primary respiratory failure, when a trial of NIV fails, in severe acidosis, and with reduced levels of consciousness and respiratory drive. The overall management of a ventilated obstetric patient is similar to the non-pregnant population. This includes adequate thromboprophylaxis, enteral feeding, sedation breaks and weaning techniques. Spontaneous
breathing modes are preferred to maintain respiratory muscle strength, but increased sedation and paralysis may be needed to optimize ventilation.\textsuperscript{47} Gastric acid suppression therapy should be routine, especially with the increased risk of gastric acid aspiration in these patients.

It is important to prevent ventilator-associated pneumonia (VAP), thought to follow bacterial colonization of the upper respiratory tract. Diagnosis based on clinical criteria has poor specificity, and microbiological samples are used including direct bronchoalveolar lavage\textsuperscript{48}, protected specimen brush\textsuperscript{49} or non-invasive endotracheal aspiration. Biomarkers such as C-reactive protein and procalcitonin\textsuperscript{50} can be useful, although they are probably less specific in the obstetric population. Methods to prevent VAP include nursing ventilated patients head-up, avoiding re-intubation and minimizing changes in ventilator circuits.\textsuperscript{51}

Strategies for weaning from mechanical ventilation, including the use of weaning protocols\textsuperscript{52}, are no different to the non-obstetric population. Percutaneous tracheostomy insertion may be indicated early in patients requiring prolonged ventilation\textsuperscript{53}, bearing in mind that the upper airway in any parturient is more oedematous and prone to contact bleeding.

**Acute respiratory distress syndrome**

Acute lung injury and ARDS are a disease spectrum with many underlying causes. The diagnosis is based on three factors: the presence of pulmonary oedema; evidence of poor oxygenation; and clinical, echo or direct evidence of normal left atrial pressure to exclude a cardiogenic cause of pulmonary oedema.\textsuperscript{54} The extent of poor oxygenation is based on a ‘P:F’ ratio of PaO₂ to FiO₂. For example, breathing air (FiO₂ 0.21), the normal range of PaO₂ would be 13–17 kPa, giving a P:F ratio of 72 kPa. With ARDS, the FiO₂ may be 0.8 and the PaO₂ only 15 kPa, giving a P:F ratio of 18.7 kPa (or 142 mm Hg), hence indicating poor oxygenation. It is always important to note the FiO₂ when measuring blood gases for this reason (Table 5).

Any pathology causing inflammation-induced injury to the alveolar–capillary interface can lead to ARDS. There is no suggestion that it is more common in pregnancy, but it may be the end result in several ‘obstetric’ diseases. Maternal mortality may be 35–60% with higher mortality post partum, and morbidity often persisting after recovery in survivors (Table 6).\textsuperscript{36}

Ventilatory strategies in ARDS are similar to the non-pregnant patient with consideration of the normal progressive respiratory alkalosis and the effects of hypoxia, hypercapnia and acidosis on the fetus. Invasive ventilation is often necessary, and is thought to contribute to a syndrome of lung injury itself. There has recently been a drive towards a ‘lung protective’ ventilation strategy to reduce the need for invasive ventilation. The components of iatrogenic ventilator-associated lung injury include those due to excess airway pressure (barotrauma\textsuperscript{55}), too high tidal volumes (volutrauma\textsuperscript{56}), airway collapse (atelectrauma\textsuperscript{59}) and local inflammation (biotrauma\textsuperscript{57}).

<table>
<thead>
<tr>
<th>Table 5. Definitions of acute respiratory distress syndrome (ARDS) and acute lung injury (ALI).\textsuperscript{54}</th>
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<tbody>
<tr>
<td>Bilateral chest X-ray infiltrates</td>
</tr>
<tr>
<td>P:F ratio &lt; 26 kPa (ARDS) or &lt;39 kPa (ALI)</td>
</tr>
<tr>
<td>Pulmonary artery wedge pressure &lt;18 mm Hg (or 2.4 kPa)</td>
</tr>
</tbody>
</table>
principles of a protective ventilation strategy in ARDS are to minimize airway pressures and to tolerate a higher pCO₂. There are, however, fetal effects of hypercapnia and acidosis, so this ‘permissive hypercapnia’ is not recommended in the obstetric patient. Furthermore, the low tidal volumes desired in ARDS in a non-obstetric patient may not be sufficient for the higher ventilatory requirements needed in pregnancy. In fact, higher tidal volumes and plateau pressures than usual may actually be necessary for this reason, and higher SaO₂ and pO₂ targets are recommended. As in any setting, positive end-expiratory pressure is useful to prevent end-expiratory lung collapse, and can improve recruitment and oxygenation of alveolar units. These effects may be offset by negative effects on cardiac filling with reduced systemic BP, exaggerated with intravascular fluid depletion.

Renal support

The incidence of acute renal failure (ARF) in pregnancy has reduced over time in both developed (1–2.8%) and developing (10–15%) countries with improvements in obstetric care, especially a reduction in septic abortions. The World Health Organization has estimated that one in eight pregnancy-related deaths in the developing world are the result of unsafe abortions and about 8% of these deaths are due to ARF. The diagnosis of ARF is complex with over 30 definitions of ARF in the literature. The RIFLE criteria were developed to provide a uniform means of classifying ARF; these have been modified recently and the term ‘acute kidney injury’ (AKI) has been introduced to encompass all causes of ARF. The classification is based on changes in serum creatinine and/or urine output over a 48-h period. It is easy to apply clinically, and importantly highlights the requirement of repeated testing of serum creatinine and the close monitoring of urine output in any patient with suspected or at risk of ARF.

Obstructive uropathy must always be excluded, and this can be difficult in pregnancy due to physiological hydronephrosis, therefore an early ultrasound can provide an invaluable baseline reference for the future when obstructive uropathy is suspected. Progesterone-induced ureteric smooth muscle relaxation plus compression by the gravid uterus leads to ureteric and renopelviceal dilatation. There is greater hydronephrosis on the right side due to physiological engorgement of the right ovarian vein and dextrorotation of the uterus.

Early recognition and treatment of AKI saves nephrons and prevents further decline in glomerular filtration rate (GFR). Serum creatinine concentration is a poor marker of GFR because it does not rise appreciably until GFR has fallen significantly. From the first trimester of pregnancy until term, there are significant increases in renal blood

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**Table 6. Causes of acute respiratory distress syndrome in pregnancy.**

<table>
<thead>
<tr>
<th>Causes specific to pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Massive haemorrhage, pre-eclampsia (especially with fluid overload), sepsis (due to chorioamnionitis, endometritis, pyelonephritis), amniotic fluid embolism, trophoblastic embolism, gastric acid aspiration</td>
</tr>
</tbody>
</table>

**Other causes**

<table>
<thead>
<tr>
<th>Other causes</th>
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</thead>
<tbody>
<tr>
<td>Sepsis (other causes), pneumonia, transfusion-related acute lung injury, trauma, inhalational injury, burns, near-drowning, acute pancreatitis etc.</td>
</tr>
</tbody>
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flow (50–85%) and GFR (40–65%); consequently, there is a parallel decline in the serum creatinine concentration. Therefore, small changes in the serum creatinine concentration can represent a significant deterioration in GFR. The calculation of estimated GFR using the modification of diet in renal disease study (MDRD) equation is not recommended in pregnancy as it overestimates GFR.

**Aetiology**

Conventionally, the major causes of AKI are grouped into three general categories: prerenal; intrinsic renal; and obstructive causes. This holds true in pregnancy, but most importantly includes the placenta-driven diseases including pre-eclampsia and HELLP (haemolysis–elevated liver enzymes–low platelets) syndrome (Table 7).

Urinary electrolyte measurements are rarely helpful clinically as they are unreliable in distinguishing between prerenal failure and acute tubular necrosis, and they do not affect management. It is useful to quantify the degree and change in proteinuria, which requires repeated random urine samples for protein:creatinine ratio measurement. This method has been validated in hypertensive and non-hypertensive pregnant patients and is comparable to 24-h collections.61

**Management of acute kidney injury**

The mainstay of treatment in ARF is aimed at minimizing damage to surviving nephrons whilst providing support until the kidney recovers. This includes the removal of tubular toxins, specific treatment of glomerular diseases and restoration of the circulation. Haemodynamic monitoring using clinical and invasive methods guides volume resuscitation and the use of vasopressors with the goal of improving perfusion pressure and urine output (>0.5–1 mL/kg/h). Failure to achieve this goal will usually become apparent at an early stage, and persistent oliguria will eventually lead to volume derangements. Oliguria can be converted to a non-oliguric state by using diuretics and low-dose dopamine, liberating valuable time prior to commencing renal replacement therapy. There is, however, little evidence to suggest that these two agents improve renal recovery times; ultimately, this depends on the number of remaining functional nephrons increasing their filtration to maintain GFR. In the postpartum patient, oliguria may

<table>
<thead>
<tr>
<th>Table 7. Aetiology of acute kidney injury.</th>
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<tbody>
<tr>
<td><strong>Pre renal</strong></td>
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<tr>
<td>Hypovolaemia (e.g. sepsis, haemorrhage)</td>
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<tr>
<td>Low cardiac output states (e.g. heart failure)</td>
</tr>
<tr>
<td>Pre-eclampsia and HELLP syndrome</td>
</tr>
</tbody>
</table>

ANCA, antineutrophil cytoplasmic antibody; GBM, glomerular basement membrane; GN, glomerulonephritis; SLE, systemic lupus erythematosus; DIC, disseminated intravascular coagulation; TTP, thrombotic cytopenic purpura; HUS, haemolytic uraemia syndrome; HELLP, haemolysis–elevated liver enzymes–low platelets.
be normal, and, as described above, inappropriate intravenous fluids can precipitate iatrogenic pulmonary oedema. Lower targets for urine output are therefore appropriate.

Metabolic derangements are an important aspect of AKI management. Hyperkalaemia is best managed by limiting potassium input, augmenting elimination with diuretics, and promoting cellular uptake with insulin and glucose boluses. Severe acidosis (pH <7.2) may require treatment with sodium bicarbonate, although avoiding hypernatraemia and excessive volume expansion. The intracellular acidosis that follows should be remembered, although it is not a problem if the spontaneously breathing patient is able to ‘blow off’ the CO₂ or if the patient is being adequately mechanically ventilated.

The indications for renal replacement therapy are the same in pregnancy as for the general population, but it is rarely required (<1 in 10 000–15 000 pregnancies). There is no clear evidence guiding dialysis dose prescription in AKI. Pregnant chronic dialysis patients achieve better fetal outcomes at higher dialysis doses (usually >20 h/week) compared with the standard regimen of 4 h thrice weekly. GFR is higher in pregnancy so the goal should be to avoid under-dialysing these patients. The aim is for more frequent and longer dialysis sessions if using haemodialysis, and in the ICU setting, continuous haemofiltration should be >35 mL/kg/h.

Hypothalamic pituitary adrenal function in critical illness

Hypothalamic pituitary adrenal function during critical illness is important and has been shown to affect outcome in septic patients. Adrenergic receptor desensitization has been demonstrated with a reduction in alpha- and beta-adrenergic receptors. Steroids have been shown to help resensitize these receptors.

The evaluation of adrenal function during critical illness is controversial. Adrenal function should still be tested, but commencement of steroid therapy should not be withheld until results are available. Currently, testing relies on random and low-dose Synacthen-stimulated serum total cortisol levels. In sepsis, adrenal insufficiency is likely when baseline cortisol levels are <10 μg/dL or the change in cortisol is <9 μg/dL, and unlikely when the Synacthen-stimulated cortisol level is ≥44 μg/dL or the change in cortisol is ≥16.8 μg/dL. Free cortisol or salivary cortisol when they become available will be more useful. Plasma aldosterone and renin level are useful when primary adrenal disease is suspected, but pregnancy-specific normal ranges must be used.

When suspected, glucocorticoid doses should be physiological with either a continuous infusion of hydrocortisone or 4–6-hourly boluses with a daily dose <200 mg. This regimen should be discontinued once there has been clinical improvement. Such patients may include those requiring >24 h or an increasing dose of vasopressors, or those with diseases such as meningococcaemia.

Neurological management

Neurological support aims to relieve pain and anxiety. Sedation is usually required for mechanical ventilation and invasive procedures. Agents include analgesics (paracetamol, opioids) and sedative-anxiolytics (benzodiazepines, propofol, haloperidol and clonidine). These are all used as needed, with consideration given to the implications on the fetus. Intubation and some modes of ventilation may also require neuromuscular blockade. Daily sedation breaks are recommended to allow a circadian sleep–wake cycle and to re-assess neurology in these patients. Very agitated patients may need
sedation if intensive monitoring and treatment is required. ICU delirium is common and difficult to manage.\textsuperscript{65}

Investigations for coma would be as in the non-pregnant population with computed tomography \(+/-\) magnetic resonance imaging, blood tests including cultures, lumbar puncture if considering meningitis, encephalitis or demyelination, and urine for toxicological screening (Table 8). Electroencephalography can be useful to assess metabolic coma and non-convulsive status, and hypoxic brain injury. Antidotes such as naloxone and flumazenil may be needed but with consideration of the risk of precipitating seizures and fetal effects. Cases of poisoning or overdose should be discussed with the local poisons unit.

For those with known epilepsy, the risk of seizures increases at the time of delivery. For women at high risk for intrapartum seizures, intravenous phenytoin or rectal carbamazepine can be given pre-emptively. In pre-eclampsia, the development of seizures defines eclampsia, and this is prevented and treated with magnesium sulphate. There are many other causes of seizures in pregnancy (including conditions listed in Table 8) as well as others including thrombotic thrombocytopenic purpura) and initial management focuses on resuscitation with control of fitting. Metabolic abnormalities including hypoglycaemia and hypocalcaemia should be corrected and intravenous magnesium sulphate given, even without known pre-eclampsia; eclampsia may present de novo. Further seizure management is with lorazepam or diazepam, then loading with intravenous phenytoin (20 mg/kg). Status epilepticus (seizures lasting \(>30\) min or multiple seizures without regaining consciousness) is managed as outside pregnancy, remembering the teratogenic effects of anticonvulsants during the first trimester, and fetal respiratory effects if peripartum.

The use of mild therapeutic hypothermia following cardiac arrest is a fairly recent treatment concept that followed two large multicentre randomized controlled trials published in 2002.\textsuperscript{66,67} It involves active cooling to 32–34°C when return of spontaneous circulation (ROSC) follows a ventricular fibrillation or ventricular tachycardia out-of-hospital arrest. The proposed mechanism is a reduction in cerebral metabolic rate which, with less free radical production and intracellular acidosis, is neuroprotective.\textsuperscript{68} However, adverse events including arrhythmias, coagulopathy, immunoparesis, and abnormal blood glucose and acid–base control may occur, and its use in pregnancy has not been reported to date.

<table>
<thead>
<tr>
<th>Table 8. Causes of coma or collapse in pregnancy.</th>
</tr>
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<tbody>
<tr>
<td>Intracerebral haemorrhage: arteriovenous malformation (AVM), Berry aneurysm, pre-eclampsia, hypertension</td>
</tr>
<tr>
<td>Subarachnoid haemorrhage</td>
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<tr>
<td>Trauma: extradural or subdural haematoma</td>
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<tr>
<td>Prolonged hypotension or hypoxia</td>
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<tr>
<td>Embolic or ischaemic stroke, venous sinus thrombosis</td>
</tr>
<tr>
<td>Pituitary apoplexy</td>
</tr>
<tr>
<td>Brain structural abnormality, e.g. tumour</td>
</tr>
<tr>
<td>Infection: abscess, meningitis, encephalitis, septic encephalopathy</td>
</tr>
<tr>
<td>Demyelination</td>
</tr>
<tr>
<td>Metabolic: hypoglycaemia, hyponatraemia, acid-base disorders, rare causes (e.g. carbamyltransferase deficiency)</td>
</tr>
<tr>
<td>Severe depression</td>
</tr>
</tbody>
</table>
Neurological intensive care

The principles of neurological intensive care management are similar to the non-pregnant setting, with prevention of secondary brain injury following an initial insult. The aetiologies of most brain insults can be subdivided into those causing coma and those leading to traumatic brain injury (TBI); the leading cause of mortality in young people. Severe cases of TBI are best managed in major hospitals with neurosurgical and neuro-intensive care facilities. Management is as for the non-pregnant woman using the airways, breathing, circulation (ABC) approach (and cervical spine control) and consideration for the fetus; immediate delivery may be indicated. Intubation and ventilation is indicated when the Glasgow Coma Scale score is <8/15, or drops by 2 points, or earlier depending on the pathology and management plan. In trauma, the secondary survey is essential in order not to miss other life-threatening injuries.

Prevention of secondary brain injury entails maintaining cerebral perfusion pressure (CPP) and normoglycaemia, and preventing complications such as infection. CPP depends on the pressure difference between MAP and intracranial pressure (ICP) within the rigid box that is the cranium (CPP = MAP-ICP). ICP is usually <10 mm Hg; an ICP >20 mm Hg may distort cerebral architecture, reduce cerebral blood flow and lead to ischaemia and oedema. It is important to maintain MAP >80–90 mm Hg to maintain CPP in the non-obstetric population, and this target may be lower in pregnancy.

Cerebral oedema may occur in TBI or other metabolic causes of coma due to disruption of the blood–brain barrier, impaired mitochondrial ability to maintain normal ionic cellular gradients, and ischaemia. ICP monitoring may be indicated, as the complication if left untreated is increasing pressure leading to coning and brain death. ICP monitoring may be indicated and depends on local practice. Initial management for raised ICP is sedation, mannitol, moderate hyperventilation and cerebrospinal fluid drainage. Further therapies include profound hyperventilation, barbiturate coma and surgical decompression. In the obstetric patient, the effects of further hypocapnia are not clear. The diagnosis of brain death is no different to the non-pregnant patient, with considerations for perimortem caesarean section for fetal survival. Somatic support of a pregnant women following brain death is rare, and organ support to preserve the fetoplacental unit must consider the predictable physiological changes that occur following brain death. These include haemodynamic instability from the excessive sympathetic discharge, panhypopituitarism, hypothermia, poor nutrition and infectious complications.

Haematological management

Haematological disorders are relatively common in pregnancy. Pregnancy is a thrombophilic state with increased levels of most procoagulants that prevent excessive maternal blood loss at the time of delivery. This and the reduction in venous flow due to the gravid uterus leads to a five-fold increased risk of venous thromboembolism during and immediately following pregnancy, and is even higher in the puerperium. Prevention of venous thromboembolic events is therefore especially relevant in obstetrics. Prophylaxis with low-molecular-weight heparin (LMWH) or low-dose unfractionated heparin, and the use of a mechanical intermittent compression device or compression stockings is essential. The anticoagulant dose of LMWH is increased as glomerular filtration is elevated; for example, the dose of enoxaparin is 1 mg/kg bd, reverting to the
usual 1.5 mg/kg od dose following delivery.\textsuperscript{75} The prophylactic subcutaneous dose is 40 mg/day in a normal-sized woman.

Anaemia is common in critical illness for many reasons. Blood transfusion targets in the non-pregnant population are $>7$ g/dL, except in those with cardiac disease who are kept $>8$ g/dL.\textsuperscript{76} Pregnancy targets should be similar, bearing in mind normal physiological anaemia.

Disseminated intravascular coagulation (DIC) is an acquired coagulopathy that follows a trigger of generalized coagulation activity. Other causes of coagulopathy are outlined in Table 9. In DIC, further consumption of platelets, clotting factors and fibrin occurs, leading to a cycle of continuing bleeding and consumption of clotting components. In pregnancy, it should be anticipated from some of the associated conditions such as massive obstetric haemorrhage (especially placental abruption with direct exposure to fetal material), pre-eclampsia, retained fetal products and amniotic fluid embolism. Sepsis is the most common overall cause in any ICU population, and other causes include transfusion reactions, trauma and drugs. Diagnosis is based on deranged clotting in an appropriate clinical setting with low fibrinogen and elevated fibrinogen breakdown products (FDPs) or D dimer levels. Management is similar to that of major obstetric haemorrhage with prompt resuscitation and fluid replacement, with identification and treatment of the underlying cause. Blood products need to be given as soon as available including packed red cells, fresh frozen plasma, cryoprecipitate and platelets. Recent developments include recombinant activated factor VIIa (NovoSeven), originally used for haemophilia and factor VII deficiency. It has been used for intractable blood loss and fulminant disseminated intravascular coagulation as it induces short-term local haemostasis. It has been used (off licence) with life-saving results in cases of massive obstetric haemorrhage.\textsuperscript{77}

**NUTRITION AND GASTROINTESTINAL MANAGEMENT**

Nutrition in pregnancy is important for the development of a healthy baby. The gastrointestinal system is the portal through which macro- and micronutrients enter

<table>
<thead>
<tr>
<th>Obstetric causes</th>
<th>Non-obstetric causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIC due to placental abruption, placenta praevia, massive obstetric haemorrhage, amniotic fluid embolus</td>
<td>DIC due to any other causes including sepsis, trauma, incompatible transfusion reaction</td>
</tr>
<tr>
<td>Thrombocytopenia, e.g. HELLP syndrome, TTP</td>
<td>Thrombocytopenia, e.g. ITP, sepsis, alcohol</td>
</tr>
<tr>
<td>Liver failure due to acute fatty liver of pregnancy</td>
<td>Liver failure due to alcohol, paracetamol overdose etc.</td>
</tr>
<tr>
<td>Bone marrow failure due to effects of shock (many causes)</td>
<td>Bone marrow failure or infiltration (many causes)</td>
</tr>
<tr>
<td>Iatrogenic</td>
<td>Pre-existing, e.g. haemophilia</td>
</tr>
</tbody>
</table>

| Hypothermia |

DIC, disseminated intravascular coagulation; TTP, thrombocytopenic purpura; HELLP, haemolysis–elevated liver enzymes–low platelets; ITP idiopathic thrombocytopenic purpura.
the body. Proteins, fats and complex carbohydrates are digested, and vitamins, minerals and water are absorbed across the gut mucosa. In pregnancy, there is an increased requirement for zinc, folate and vitamin B12 in the first trimester, and calories in the second and third trimester. Nutritional support is required to meet the increased metabolic demand and limited nutritional reserve during critical illness. However, despite extensive research, many areas in this field of critical care medicine remain controversial, due to a lack of well-controlled randomized trials.

The availability of functioning small bowel is vital and should prompt early feeding, preferably via the enteral route. Enteral nutrition is cheap and safe, but can be complicated by aspiration and poor gastric emptying, which results in poor absorption and under-feeding. Increased progesterone levels in pregnancy cause smooth muscle relaxation. This results in an increased likelihood of aspiration and constipation due to the reduced oesophageal sphincter tone and bowel peristalsis. Aspiration can be prevented by a 45° head-tilt position and confirming the nasogastric tube placement radiologically. Good absorption of feed often requires the use of prokinetic agents to promote gastric emptying when residual gastric volumes are high, and laxatives and enemas to prevent constipation. If poor absorption is a problem, drugs given via the nasogastric tube should also be considered to be poorly absorbed, and prompt conversion to the intravenous route should be instituted. Some drugs require enteral feed to be discontinued to ensure good uptake and effective absorption, such as the anti-convulsive drug phenytoin.

Protocols have been developed and are implemented by nurses to ensure that adequate enteral nutrition is delivered early and effectively. The failure to deliver 25% of a patient’s calculated calorific requirement has been shown to result in increased mortality and infection rates. Protocol-directed regimens have been shown to reduce the incidence of under-feeding; however, it remains a significant problem for many patients due to frequent and often avoidable interruptions.

Total caloric requirements can be either estimated or calculated, and are often estimated at 25–35 kcal/kg/day. Calculations are required at extremes of weight and performed by dieticians. The recommended nutritional requirements of a septic patient are 25 total kcal/kg/day, given in three forms: protein 1.3–2.0 g/kg/day; glucose 30–70% of non-protein calories; and lipids 15–30% of non-protein calories.

The H2 receptor blocker ranitidine is used as prophylaxis against stress ulceration; there is no evidence to suggest that proton pump inhibitors are superior. The National Institute for Health and Clinical Excellence recommends that parenteral nutrition should be limited to 50% of the calculated calorific requirement, and it has been shown to be less harmful than first thought. It is useful when the small bowel is being rested or not functioning for prolonged periods. Glycaemic control has also been shown to affect outcome in sepsis, and the Surviving Sepsis Campaign guidelines advise controlling blood glucose <8.3 mmol/L. This should be achieved using insulin infusions and close monitoring of blood glucose. Micronutrients and electrolytes, e.g. magnesium, iron, copper, zinc and selenium, are necessary in small amounts. Phosphate is important since it is required for normal metabolic processes resulting in the formation of ATP. Hypophosphataemia results in reduced contractility of skeletal muscles including respiratory muscles, which can lead to difficulties weaning from ventilatory support. Other micronutrients include fat-soluble (vitamins A, carotene) and water-soluble vitamins (vitamins B, C, D and E). The precise requirements for specific vitamins remain unclear, although several studies have shown extremely low circulating concentrations. In pregnancy, the supplementation of folate should be continued.
Early goal-directed therapy

Haemodynamic goal-directed therapy (GDT) was first used in sepsis and has since been introduced in the peri-operative care setting, targeting oxygen delivery as the ‘goal’. Original studies of sepsis in the late 1980s noted that survivors of sepsis had supranormal levels of oxygen delivery (DO2) compared with controls.\(^8\) However, targeting high DO2 levels did not initially appear to improve outcome.\(^8\) It became apparent from a meta-analysis of all the optimization trials that the timing of such interventions was crucial\(^8\) where the earlier interventions did in fact reduce mortality. There are evidently two phases to sepsis. The early phase is characterized by low oxygen delivery, high lactate and low SvO2 levels. This phase is associated with high morbidity and mortality if left untreated, but may be reversible if targeted early.\(^8\) In comparison, the later phase of ‘established’ sepsis is more hyperdynamic with a higher SvO2, CO and DO2 (Table 10).\(^8\)

This early work led to a landmark study of sepsis before admission to ICU. Rivers et al studied patients with severe sepsis and septic shock over 6 h following presentation to the emergency department (ED).\(^10\) Patients with systemic inflammatory response syndrome criteria and BP < 90 mm Hg or serum lactate > 4 mmol/L were randomized to standard ED care or the early GDT protocol with continuous central venous oxygen saturations (ScvO2) monitoring with goals as follows: CVP 8–12 mm Hg, MAP > 65 mm Hg, urine output (UO) > 0.5 mL/kg/h, ScvO2 > 70% (or SvO2 > 65%). If the ScvO2 was below target, protocolized manoeuvres were undertaken to increase DO2. These included fluid boluses, giving packed cells to increase haematocrit > 30% and using vasopressors or inotropes. The other important feature in the trial was the use of antibiotics within 1 h. The overall results from the early GDT protocol indicated a significant mortality benefit (30.5% for early GDT vs 46.5% for standard care). The important message from this is that survival in sepsis does appear to be influenced by the care in the first few hours, and that sepsis appears to have an early reversible phase. It has revolutionized the importance of early diagnosis and accessibility to critical care facilities for patients admitted with septic shock and severe sepsis. This principle has been extrapolated to the peri-operative care of patients.\(^8\)

Cardiopulmonary resuscitation in pregnancy

Cardiac arrests in pregnancy are fortunately rare, occurring in approximately one in 30 000 late pregnancies. They are less likely to have a primary cardiac cause compared

<table>
<thead>
<tr>
<th>Table 10. Definitions of sepsis syndromes.(^8)</th>
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<tr>
<td><strong>Infection</strong></td>
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<tr>
<td><strong>SIRS</strong></td>
</tr>
<tr>
<td><strong>Sepsis</strong></td>
</tr>
<tr>
<td><strong>Severe sepsis</strong></td>
</tr>
<tr>
<td><strong>Septic shock</strong></td>
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SIRS, systemic inflammatory response syndrome.
with cardiac arrests outside pregnancy. The most common reason for syncope is the supine hypotension syndrome, and management of patients in the left lateral position is essential. Other common causes of cardiac arrest in pregnancy are shown in Table 11.

The concept of a ‘chain of survival’ with basic and advanced life support is as important in pregnancy as in the general population. It includes early recognition and call for help, early cardiopulmonary resuscitation (CPR), early defibrillation and postresuscitation care. The structured ABC, airway-breathing-circulation approach in cardiac arrest underpins the principles of basic and advanced life support with the goal of establishing a spontaneous return of circulation.

CPR in pregnancy is complicated by both physiological and physical changes that are well established late in pregnancy. They affect the quality of CPR that can be delivered, and increase the possibility of complications. Each component is considered below, including the important differences in pregnancy.

### Airway

Simple airway manoeuvres remain the same as for the general population. Difficult intubations are more common and effective pre-oxygenation is essential. Insertion of an advanced airway at an earlier stage and with a 0.5–1 mm smaller endotracheal tube is recommended. The short obese neck and full breasts make insertion of the laryngoscope more problematic. Short-handled laryngoscopes, blades mounted greater than 90° and dismountable blades first inserted into the mouth can all help to overcome these difficulties. A laryngeal mask airway may be needed in cases of failed intubation, although cricoid pressure should be released and re-applied after insertion and inflation of the mask.

### Breathing

Mouth-to-mouth and bag and mask ventilation should be performed without a pillow and the head fully extended. Ventilation can be hampered by flared ribs, raised diaphragm, reduced chest compliance and difficulties seeing the chest rise. These along with greater oxygen demand and reduced FRC lead to rapid desaturation with inadequate ventilation. The problems of ventilation can be compounded by aspiration, which is more likely in late pregnancy due to the incompetent gastro-oesophageal sphincter and raised intragastric pressure.

### Circulation

Femoral intravenous access for resuscitation drugs is not advised, as central maternal delivery will not occur until the fetus is delivered. Chest compressions should be

<table>
<thead>
<tr>
<th>Obstetric causes</th>
<th>Non-obstetric causes</th>
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<tr>
<td>Pulmonary embolism</td>
<td>Trauma</td>
</tr>
<tr>
<td>Amniotic fluid embolism</td>
<td>Septic shock</td>
</tr>
<tr>
<td>Massive blood loss</td>
<td>Drug overdose</td>
</tr>
<tr>
<td>Complications of pre-eclampsia</td>
<td>Acute myocardial infarction</td>
</tr>
<tr>
<td>(and magnesium toxicity)</td>
<td>Severe asthma</td>
</tr>
<tr>
<td>Uterine inversion</td>
<td>Local anaesthetic toxicity</td>
</tr>
<tr>
<td>Aortic dissection</td>
<td>Failed intubation, high spinal block</td>
</tr>
</tbody>
</table>

Table 11. Causes of cardiac arrest in pregnancy.
performed at the standard rate of 100/min and a ratio of 30:2. Hands should be po-
sitioned further up the sternum because abdominal contents are displaced upwards
by the gravid uterus. The patient must be rolled into the left lateral position. This
should be up to 30° or there is a tendency to roll into the full lateral position. This
angle is ideal for effective chest compression, and aids displacing the uterus off the in-
ferior vena cava. This manoeuvre, along with raising the patient’s legs, will improve ve-
nous return. One technique to achieve this is the ‘human wedge’, whereby the patient
is tilted on to a rescuer’s knees to provide a stable position for CPR.

Defibrillation and drug administration is similar in pregnancy as for the general pop-
ulation. Defibrillation will not deliver significant current to the fetus, but any fetal mon-
itoring electrodes must be removed. Adhesive defibrillation pads have removed the
difficulties of applying the paddles in the correct position, normally affected by the
full breasts and left lateral position adopted. Excessive magnesium sulphate used to
treat and prevent eclampsia can contribute to cardiac arrest. Empiric calcium should
be given and can be life saving.

Perimortem caesarean section

Failure to achieve ROSC after 5 min of CPR should prompt consideration of perimor-
tem delivery. This should be considered by the team leader at the onset of cardiac ar-
rest. The greatest chance of infant survival is in pregnancies >24 weeks of gestation as
neonatal resuscitation can commence. It is obviously an aggressive procedure, but in-
fant and maternal survival may depend on it. In pregnancies >20 weeks, emptying the
uterus after this will improve CO by 60–80% of prepregnancy levels, allowing venous
return and improving chances of ROSC, improving maternal and fetal outcome. Car-
diac compressions are also more effective after delivery. In pregnancies <20 weeks,
the gravid uterus is unlikely to have detrimental compressive effects. In pregnancies
<23 weeks, infant survival is unlikely; if done, it should be for maternal survival.

Between 1975 and 2000, there were 56 postmortem caesarean deliveries with six
neurologically normal surviving infants (survival rate 10.7%). Eight infants were deliv-
ered alive but died in the neonatal period. Of the 40 perimortem deliveries, 25 sur-
vived neurologically intact (survival rate 62.5%).

Post-resuscitation care

ROSC is an important step in resuscitation, but this must be followed by meticulous
postresuscitation care to increase the chance of a return to normal cerebral function.
It focuses on the re-assessment of ABCDE to ensure good oxygenation, stable cardiac
rhythm and BP. Once established, the patient can be transferred to a critical care area
for ongoing postresuscitation care.

SUMMARY

It is important to understand the aims of managing critically ill obstetric patients in
many areas of clinical medicine, surgery and anaesthesia. The most common reasons
for UK obstetric ICU admissions are pre-eclampsia, sepsis and haemorrhage. The ma-
ternal physiological differences make a significant impact on the assessment and man-
age, and must be considered at all times, especially the supine hypotension
syndrome in positioning and resuscitation scenarios. Additional considerations are
for fetal wellbeing and appropriateness for delivery, which may be life saving for the
mother. The developments and trials in critical care medicine over the last 50 years have not included obstetric patients specifically. However, with the changes in maternal physiology borne in mind, there are no reasons why the principles should differ greatly. When considering haemodynamic management, the requirement for a high maternal CO should be remembered. The low colloid oncotic pressure leads to an increased tendency to develop iatrogenic pulmonary oedema, and several obstetric pathologies tend to increase alveolar capillary permeability, compounding the problem. Oliguria post delivery, especially in pre-eclampsia, should not usually be managed with a fluid challenge. Airway management may be challenging with altered anatomy.

### Practice points

**General supportive care**
- immediate resuscitation of the mother is paramount for maternal and fetal survival
- consider fetal age at an early stage; monitoring/assessment and delivery if indicated
- early identification of warning signs of critical illness
- always plan in advance with the multidisciplinary team, where possible, such as booking an ICU bed for expected high-risk deliveries

**Haemodynamic management**
- remember the supine hypotension syndrome
- beware of iatrogenic pulmonary oedema with fluid challenges
- labour is a high-risk time for cardiac patients, with fluid shifts for up to 72 h post partum

**Cardiopulmonary resuscitation**
- airway: pregnant women may be very difficult to intubate (need skilled anaesthetist). Need smaller endotracheal tube, short-handled laryngoscope blade and ‘difficult intubation’ equipment
- breathing: may be difficult to ventilate. Increased risk of gastric acid aspiration
- circulation: always use lateral position to avoid the supine hypotension syndrome. CPR cycles and drugs given as outside pregnancy, remembering that MgSO4 toxicity can lead to cardiac arrest (give empiric calcium intravenously)
- perimortem caesarean section may be necessary and should be considered at the start of CPR

### Research agenda

- more on the mechanism of ARDS in pre-eclampsia, and how to avoid iatrogenic pulmonary oedema
- ideal ventilatory targets throughout pregnancy
- short-term effects of fetal hypoxia, hypercapnia and acidosis
and high oxygen consumption, and rapid oxygen desaturation may occur. Ventilatory management may be difficult for this reason and higher pressures may be needed. Some of the recommended ARDS ventilatory strategies are probably not appropriate as fetal haemoglobin binds oxygen less well when acidotic. Overall, critical care management in obstetrics is mostly similar to a non-obstetric setting, applying the changes in maternal and fetal physiology in each case. High-risk patients should be identified early, with appropriate planning and involvement of the multidisciplinary team.

ACKNOWLEDGEMENTS

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