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Understanding shock

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Abstract

Shock is a failure of the circulation to deliver oxygen and nutrients to the tissues. It is common in children, but understanding its causes and pathophysiology can lead to rational decisions about therapy which may lead to improvement in outcome. This review aims to give the reader a comprehensive understanding of the main classification, causes and pathophysiology of shock in children, with a guide to recognition and monitoring, leading to an understanding of a rational approach to therapy.

Keywords inotrope; monitoring; oxygenation; resuscitation

Introduction

Shock is a complex clinical syndrome characterized by a state of acute circulatory dysfunction in which the normal relationship between oxygen demand and oxygen supply is impaired.¹ Consequently, the cardiovascular system fails in its primary function of substrate delivery and metabolite removal, resulting in anaerobic metabolism and tissue acidosis. In general, all shock states eventually lead to decreased delivery or impaired utilization of essential cellular substrates and, finally to loss of normal cellular function.

Shock is a progressive process characterized by three different stages. In the early, compensated stage, a number of neurohormonal compensatory physiological mechanisms act to maintain blood pressure and preserve adequate tissue perfusion. At this stage, shock may be reversible with appropriate therapeutic intervention. However, when these compensatory mechanisms fail, shock progresses to an uncompensated stage. In the irreversible stage, shock progresses to severe organ and tissue injury, which is unresponsive to conventional therapy, eventually leading to multiple organ failure and death of the patient.

Shock is a clinical diagnosis, but its recognition remains problematical in children. In guidelines published by the American College of Critical Care Medicine, Carcillo et al defined septic shock in children as tachycardia with signs of decreased peripheral perfusion, including reduced pulse volume, prolonged capillary refill time (CRT) of > 2 s, mottled or cool extremities, altered

alertness and decreased urine output.² Hypotension is a sign of late and decompensated shock in children and should not be relied upon to make the diagnosis.

Shock should be recognized by clinical and laboratory signs that include tachypnoea and tachycardia, peripheral vasodilation (warm shock) or cool extremities (cold shock), altered mental status, hypothermia or hyperthermia, together with reduction of urine output, metabolic acidosis and increased blood lactate.

Classification of shock

As circulatory function is dependent on blood volume, vascular tone and cardiac function, shock states may result from abnormalities in one or more of these factors, or from cellular metabolic disturbances due to inability to utilize substrates delivered by the circulation. Five main types of shock are described (Table 1). This categorization is an oversimplification, as several mechanisms may occur in the same patient. The end result is failure to provide energy substrates to meet the metabolic demand of the tissues.³

Classification of shock

Type	Clinical syndrome
Hypovolaemic	Haemorrhage Non-haemorrhagic fluid depletion: <ul style="list-style-type: none"> • Vomiting • Diarrhoea • Severe burn • Internal sequestration • Diabetes • Nephrotic syndrome • Other forms of dehydration
Cardiogenic	Myocardial infarction Severe congestive failure Cardiac surgery Valvular disease/coarctation Dysrhythmias Myocarditis/cardiomyopathy Cardiopulmonary bypass Septic shock Drug intoxication
Obstructive	Cardiac tamponade Valvular disease/coarctation Pneumothorax Pulmonary embolism
Distributive	Septic shock Toxic shock Anaphylaxis Neurogenic shock Acute adrenal failure Drug intoxication
Dissociative	Poisoning, e.g. cyanide, methaemoglobin, carbon monoxide Profound anaemia

Table 1

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Quantitative shock (decreased oxygen delivery)

Decreased flow (hypovolaemic, cardiogenic shock)

In hypovolaemic, cardiogenic and obstructive forms of shock, the primary defect is a fall in cardiac output, leading to hypoperfusion, hypotension and anaerobic metabolism.

Hypovolaemic shock is the most common type of shock in children and is a result of decreased circulating volume (absolute or relative hypovolaemia). Hypovolaemia is 'absolute' when due to dehydration from loss of extracellular fluid, blood or plasma; and 'relative' when intravascular fluid volume is inadequate to compensate for loss of vascular tone, as in sepsis or anaphylaxis, or due to vasodilating agents.

Cardiogenic shock is caused by a decline in cardiac output secondary to myocardial damage and/or dysfunction. This can be due to myocardial injury (infectious or ischaemic) or obstructive lesions (increased right ventricular afterload, increased left ventricular afterload, cardiac tamponade) and/or from lack of ventricular filling (decreased right ventricular or left ventricular preload, valvular lesions, decrease in filling time due to tachyarrhythmias).

Decreased oxygen content (haemorrhagic shock, acute hypoxaemic respiratory failure, poisoning)

Haemorrhagic shock is usually a result of hypovolaemia and anaemia. When anaemia is associated with haemorrhage, the decrease in oxygen delivery (DO_2) is substantially greater than either insult alone. Decreased oxygen-carrying capacity of haemoglobin (Hb), and therefore inadequate DO_2 , may also cause shock. For instance, with carbon monoxide (CO) poisoning, decreased DO_2 results from competitive binding of CO in preference to O_2 , and is exacerbated by abnormal O_2 utilization, as CO interferes with oxidative phosphorylation, resulting in a decreased oxygen extraction ratio (O_2ER). In this case, shock is both distributive and quantitative. In any respiratory cause of acute hypoxia, decreased arterial oxygen saturation (SaO_2) leads to a decrease in DO_2 as soon as the increase in cardiac output is unable to compensate for metabolic needs.

Distributive shock (decreased oxygen extraction)

Distributive shock often coexists with hypovolaemic and/or cardiogenic shock. Distributive shock results from abnormalities in flow distribution among organs, secondary to impaired vasomotor tone, such as occurs in sepsis and anaphylaxis. In addition in sepsis, a decrease in capillary recruitment secondary to altered vascular reactivity, disseminated intravascular coagulation, endothelial cell dysfunction or increased blood cell adhesiveness, together with mitochondrial dysfunction, may be present. These changes contribute to the inability fully to utilize oxygen that is delivered. Spinal cord injury is a specific form of distributive shock that leads to profound haemodynamic changes. A sudden loss of sympathetic outflow from the spinal cord leads to a sudden decrease in total peripheral resistance and cardiac output.

Pathophysiology of shock

Circulatory failure results in a decrease in DO_2 to the tissues and is associated with a decrease in cellular partial pressure of oxygen (PO_2). When a critical PO_2 is reached, oxidative phosphorylation is limited by lack of oxygen, leading to a shift from

aerobic to anaerobic metabolism. The result is a rise in cellular and blood lactate concentration and a concomitant metabolic and lactic acidosis.

DO_2 depends on two variables: the arterial oxygen content (CAO_2) and cardiac output. CAO_2 is the product of Hb content, arterial SaO_2 and Hb oxygen-carrying capacity. In turn, cardiac output depends on heart rate and stroke volume, which is determined by myocardial contractility and ventricular preload and afterload. In children, cardiac output depends more on heart rate than on stroke volume because of myocardial immaturity.

Inadequate tissue energetic metabolism may derive from an increase of total body oxygen consumption (VO_2), despite normal DO_2 . Oxygen demand varies according to tissue type and time.⁴ Although oxygen demand cannot be measured or calculated, VO_2 and DO_2 can both be quantified, and are linked by the relationship:

$$VO_2 = DO_2 \times O_2ER \text{ (oxygen extraction ratio)}$$

Under normal conditions, oxygen demand equals DO_2 . When demand increases, DO_2 must adapt and increase. During circulatory shock or hypoxaemia, as DO_2 declines, VO_2 is maintained by a compensatory increase in O_2ER . However, if DO_2 falls further, a critical point is reached and O_2ER can no longer increase to compensate for the fall in DO_2 . During septic shock, tissue oxygenation may be inadequate even in the presence of normal blood flow due to a major increase in metabolic demand and impaired oxygen extraction.

The pathophysiological consequences of cardiogenic and hypovolaemic shock are related predominantly to acute deficiency of oxygen, whereas the pathophysiological effects of septic shock result largely from the overwhelming production of inflammatory mediators. In septic shock there is a complex interaction between pathological vasodilatation, relative and absolute hypovolaemia, direct myocardial depression and altered blood flow distribution, which occur as a consequence of the inflammatory response to infection. The excessive inflammatory response is then responsible for haemodynamic compromise and widespread tissue ischaemia, leading to multiple organ dysfunction.

Clinical assessment

To apply any therapeutic intervention, early recognition of shock is crucial. Previously well children with intact cardiovascular homeostatic mechanisms can compensate extremely well during hypoperfusion states. For this reason, it may be difficult to differentiate the early phases of compensated shock. Constant vigilance and repeated re-evaluation is therefore required.

The early diagnosis of shock requires knowledge of the conditions that predispose children of different ages and co-morbidities to shock. For instance, a history of congenital heart disease, immunodeficiency, trauma, surgery, toxin ingestion or allergies is important.

In neonates, the maternal and birth history is required, especially with regard to timing and duration of rupture of membranes, maternal fever, blood loss, fetal distress and other obstetric information. In the case of trauma, history regarding the mechanism and timing of injury, whether excessive blood loss has occurred, and the level of consciousness before hospital

arrival is vital. A history of immunodeficiency, use of immunosuppressive agents, duration and height of fever, and associated features, such as lethargy, vomiting, diarrhoea, decreased oral intake and decreased level of consciousness or awareness, may suggest infection and the possibility of septic shock or dehydration. Other details, such as environmental exposure, drug ingestion, previous medical history and allergies, are also important.

Physical examination

As children often will maintain their blood pressure until they are very severely ill, children may be shocked despite the absence of systemic hypotension. However, once hypotension occurs, cardiovascular collapse is likely to follow.

Shock in children can be recognized by clinical and laboratory signs that include altered mental status, tachypnoea and tachycardia, hypothermia or hyperthermia, and changes in peripheral perfusion [vasodilation (warm shock) or cool extremities (cold shock)], together with reduction of urine output, metabolic acidosis and increased blood lactate.

In the early, compensated stage, homeostatic mechanisms maintain vital organ perfusion. Blood pressure, urine output and cardiac function may all appear normal; however, early cellular metabolic alterations are taking place which may be detected by the presence of metabolic acidosis or increased lactate. In decompensated shock, circulatory compensation fails because of dysoxia, ischaemia, endothelial cell injury and dysfunction. Eventually, widespread abnormalities occur in all organ systems, leading to multiorgan failure. When this process has caused such widespread organ dysfunction, death is inevitable despite support.

Poor tissue perfusion may be manifested clinically by changes in body surface temperature, prolonged capillary refill time (CRT) and impaired organ function (oliguria, altered sensorium). Decreased skin perfusion and temperature reflects a predominance of the sympathetic neurohumoral response to hypovolaemia. Clinical signs of poor peripheral perfusion consist of cold, pale, clammy and mottled skin, associated with a prolonged CRT. In particular, skin temperature and CRT have been advocated as an indicator of the adequacy of peripheral perfusion.⁵

Peripheral CRT has become widely accepted as a reflection of intravascular volume, especially in children and in the assessment of trauma. A value < 2 s at normal ambient temperature is considered adequate. Prolonged CRT in children has been found to be a good predictor of dehydration, reduced stroke volume and increased blood lactate levels.⁶

Therefore, monitoring skin temperature and CRT as well as heart rate, blood pressure and urine output are valuable during circulatory shock, and should be the first approach in the assessment of any critically ill patient.

Laboratory markers of shock

Serial blood gases to evaluate base excess and blood lactate are widely used to complement clinical assessment by quantifying the extent of tissue hypoperfusion and to provide useful trends with which to titrate therapy. Normalization of blood pressure may not indicate reversal of the shock state in a patient who has ongoing metabolic acidosis and/or elevated lactate.

The adequacy of regional perfusion is usually assessed by evaluating indices of specific organ function. These include coagulation abnormalities, disturbed renal function with increased blood urea and creatinine, altered liver function with increased levels of transaminases, lactate dehydrogenase and bilirubin, and altered gut perfusion, manifest by ileus or malabsorption.

In the clinical setting mixed venous O₂ saturation (SvO₂) can be useful in assessing the whole-body VO₂–DO₂ relationships. SvO₂ is dependent on cardiac output, oxygen demand, Hb concentration and arterial oxygen saturation. The normal SvO₂ value is 65–75% and it is measured in patients using a pulmonary artery catheter. Recent studies have used central venous oxygen saturation (ScvO₂) as a surrogate for SvO₂ to detect global O₂ deficiency.⁷ ScvO₂ is becoming increasingly popular as an alternative to SvO₂ because the former approximates to SvO₂ and can be obtained from a central venous catheter (superior vena cava). A decrease in S(c)vO₂ of 5% from its normal value represents a significant fall in cardiac output and/or an increase in oxygen demand. Prompt rapid intervention such as fluid resuscitation, inotropic therapy or red cell transfusion to increase oxygen delivery to the tissues should be instituted. In sepsis, abnormalities in oxygen extraction or utilization due to mitochondrial dysfunction may be present, when elevated SvO₂ associated with severe metabolic acidosis may occur.

The implication is that the strategy for managing shock relies on early estimation of O₂ deficit, rapidly followed by corrective therapy and ongoing monitoring.

Therapeutic principles (Figure 1)

Initial management

Recent studies provide further evidence that early normalization of haemodynamic status can affect overall outcome, therefore appropriate recognition and management of shock in the emergency department becomes even more essential. Initial management should focus on interpreting and treating haemodynamic derangements, with targeted diagnostic and therapeutic interventions aimed at improving tissue perfusion and restoring a balance between DO₂ and demand. This initial management has been labelled ‘early goal-directed therapy’ and includes prompt fluid resuscitation, appropriately targeted vasoactive therapy, early empiric antimicrobial therapy and appropriate and continuous monitoring of haemodynamic status. In the landmark study of Rivers et al, there was lower mortality in adults with sepsis when they were aggressively treated to achieve haemodynamic and oxygenation goals using fluid administration, early red-cell transfusions and early vasoactive therapy.⁸ In addition, support of the airway and breathing is essential to maximize DO₂. Supplemental oxygen should be administered to all patients presenting with signs of shock and early tracheal intubation may be necessary.

Volume resuscitation

Fluid challenge is the first step in therapy. The goal is to optimize left ventricular preload and improve DO₂ by increasing cardiac output. However, this may increase the risk of pulmonary oedema. It has been reported that up to 60 ml/kg fluid may be given in the first hour of therapy to children with septic shock, without increasing the risk of pulmonary oedema, while resulting in a consequent improvement in outcome.⁹

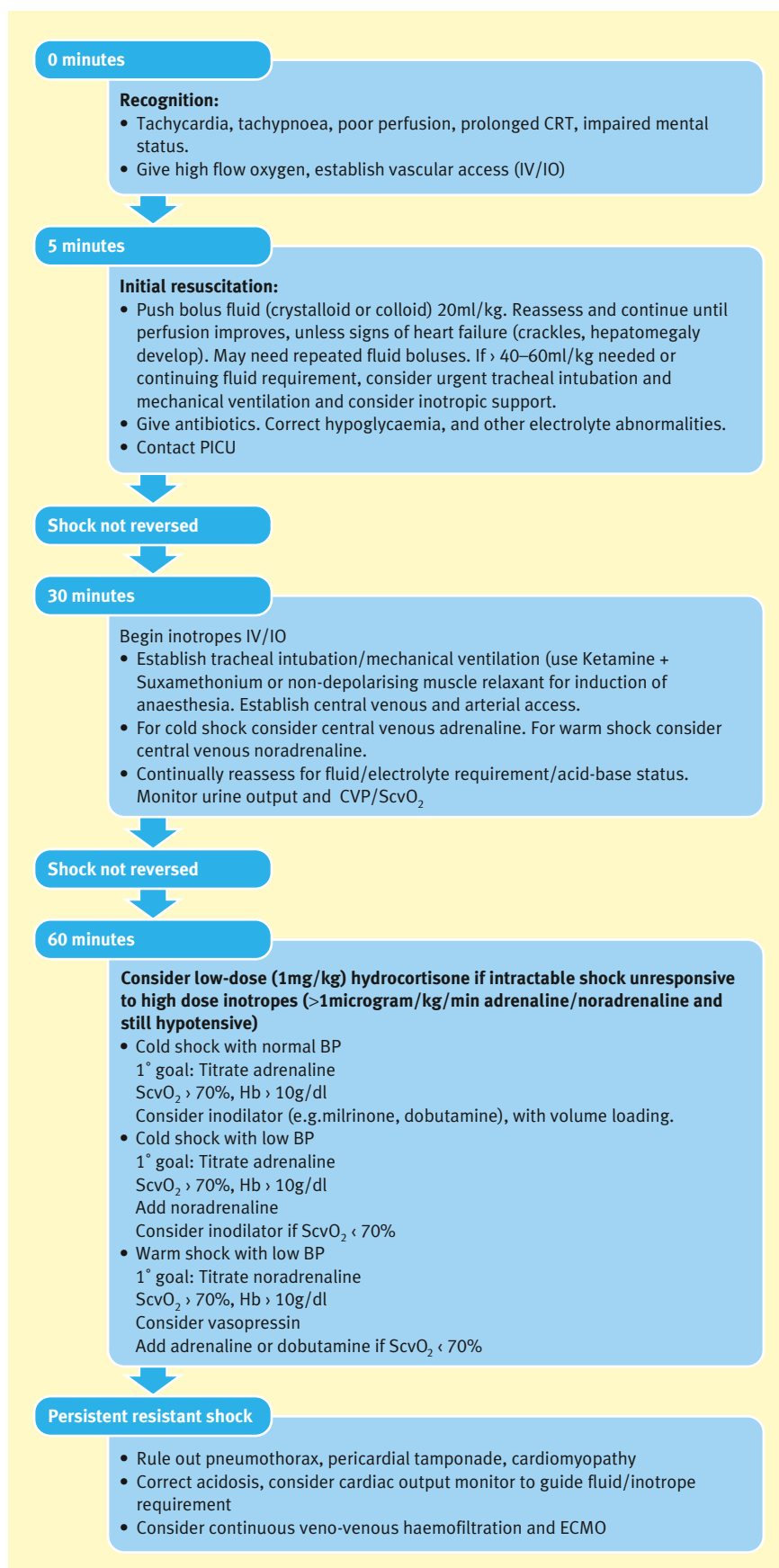


Figure 1 Time-dependent algorithm for the management of shock in children.

Fluid requirement is usually determined by assessment of clinical parameters, such as a heart rate, blood pressure, peripheral perfusion and urine output. These may be supplemented by invasive monitoring of central venous and arterial pressure, as well as biochemical parameters of global perfusion, such as ScvO_2 , blood lactate and base deficit.

The choice of fluid for resuscitation is also a subject of intense debate. A large, randomized, controlled study in adult patients in intensive care showed that use of either 4% human albumin solution (HAS) or normal saline for fluid resuscitation resulted in similar outcomes at 28 days.¹⁰ However, in subgroup analyses of patients included in this study, HAS seemed to have a protective effect in patients with sepsis, and normal saline seemed to have a protective effect in patients with traumatic brain injury. The reasons for these subgroup findings are unclear, but need to be examined in future studies.

In one analysis of children with dengue shock syndrome, no difference was seen between patients resuscitated with crystalloid or colloid solutions.¹¹ The recently published 'surviving sepsis' guidelines suggest initial resuscitation with infusion of crystalloid, with boluses of 20 ml/kg over 5–10 min, titrated to clinical estimation of CO.¹²

Fluid refractory shock is defined as the persistence of shock after the administration of sufficient fluids to achieve a central venous pressure of 8–12 mmHg and/or signs of fluid overload (hepatic congestion, pulmonary oedema). Additional therapy such as vasopressors/inotropes should be administered.

Vasoactive agents

Catecholamines help restore perfusion pressure and cardiac output, improving DO_2 .

The choice of vasoactive agent is determined by clinical examination.¹³ In vasodilated ('warm') shock (bounding pulses, warm extremities, normal CRT), the use of vasoconstrictor agents [e.g. noradrenaline (norepinephrine)] appear beneficial. In cases with persistently low systemic vascular resistance (SVR) despite noradrenaline, use of vasopressin has been described; however, this may significantly elevate afterload and compromise cardiac output. There is no clear evidence to support the use of vasopressin in children.

A predominantly poor cardiac output state, referred to as 'cold shock' and clinically manifested by weak pulses, cool extremities and prolonged CRT, is associated with vasoconstriction and consequent increased afterload. Using inotropic agents such as dobutamine, adrenaline (epinephrine) or milrinone would appear to be most beneficial. Careful assessment of cardiac output, SVR and blood pressure after instituting vasoactive therapy helps guide further management.

Antibiotic therapy

Ample evidence suggests that early administration of appropriate antibiotics and control of source of infection reduces mortality in patients with sepsis. Antibiotics should be administered within 1 h of recognition of sepsis. The choice of antibiotics is vital and should be guided by the susceptibility of likely infecting pathogens, as well as any specific knowledge about the patient, including underlying disease and the clinical syndrome.

Children with severe sepsis or septic shock require broad-spectrum antimicrobial therapy until the causative organism and

its antibiotic susceptibilities are available. The antimicrobial regimen should be reassessed after 48–72 h on the basis of microbiological and clinical data, with the aim of narrowing the antibiotic spectrum to reduce the risk of development of antimicrobial resistance, toxicity and costs.

Blood replacement

Usually, blood replacement is not required unless shock is due to acute haemorrhage or anaemia. However, patients with cardiovascular disease, low cardiac output, severe hypoxaemia, low SvO_2 and persistent lactic acidosis may need higher Hb. An Hb of at least 8–10 g/dl is recommended in this situation, with the understanding that there are limited data for this practice.

Other therapeutic principles

Although laboratory studies rarely impact the management of shock in the first hour of therapy, patients should be routinely assessed for haematological abnormalities, metabolic derangements or electrolyte abnormalities that may contribute to morbidity. Recognition and treatment of metabolic abnormalities, such as hypoglycaemia, hypocalcaemia and hypokalaemia, may improve outcome.

Replacement low-dose steroid therapy may be beneficial in some patients with septic shock and evidence of adrenal hyporesponsiveness, especially in those with high or increasing requirements for inotropes. This benefit has not yet been demonstrated in children. However, similar adrenal hyporesponsiveness has been demonstrated,¹⁴ and stress doses of steroids are now commonly used in children who require high-dose inotropes, without clear evidence of their benefit. A recent study in adults with sepsis, however, has not confirmed benefit from low-dose steroid administration.¹⁵

In case of refractory shock that cannot be supported by conventional therapies, the use of haemofiltration or extracorporeal membrane oxygenation (ECMO) may be considered.

Conclusion and future directions

Shock is a clinical diagnosis. The mainstay of therapy is early recognition of the seriously ill child before shock progresses to irreversibility. Once shock is present, urgent attempts must be made to reverse it. Management is dependent on understanding the causes of shock and giving both cause-directed and goal-directed therapies. Support measures that counteract hypoxaemia and impaired tissue perfusion should be undertaken. Frequent reassessment to anticipate issues that may contribute to circulatory collapse, progression of shock or insufficient therapy are needed. Prompt transfer to a paediatric intensive care unit for continued haemodynamic monitoring and further organ support can improve outcome. International guidelines for adults, with definition of specific goal-directed therapies and evidence-based targets for sepsis and septic shock, have been recently published. However, defining the optimum treatment for shock in children is an evolving process and only with well-controlled, randomized trials for children with shock states will we be able to evaluate the most appropriate and effective aspects of therapy. ♦

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Practice points

- Recognition of shock in children is difficult
- Early, aggressive fluid resuscitation leads to improvement in outcome
- Failure of shock reversal leads to increased mortality
- Early intubation, ventilation, monitoring of central venous oxygen saturation and appropriate manipulation of the circulation can lead to improvement in outcome
- Many of the currently used therapies do not have a good evidence base for their continued use

Advanced paediatric life support in practice

Fiona Reynolds

Abstract

Paediatric resuscitation guidelines provide a framework allowing resuscitation teams to work in a coordinated fashion to provide timely resuscitation to the collapsed child. Effective resuscitation systems include early recognition of sick children, communication systems, training of parents and healthcare professionals, provision of equipment and direct clinical care to the critically ill child. Clinical outcomes may be improved by early recognition and timely intervention to prevent further deterioration. If collapse has occurred effective and timely management is essential to optimize outcomes.

Keywords early warning score; life support; paediatric; resuscitation

Introduction

Paediatric cardiac arrest is rarely a primary event and usually occurs after gradual deterioration. The overall outcomes are very poor. Therefore, the emphasis of resuscitation training is on early recognition and treatment of the critically ill child, before respiratory or cardiac arrest occurs.

Early identification of the critically ill child is usually dependent on clinical evaluation by parents, nursing staff or doctors. Newly developed early warning scoring systems are being used to aid identification of the critically ill child. The early warning scores in use at the time of writing are based on expert opinion. Validated scoring systems are likely to be published soon. However, a scoring system is only as good as the response it elicits. In some hospitals, medical emergency teams (MET) have been introduced to assess and treat patients who have reached a threshold on the local early warning score. Early evidence suggests that MET teams reduce the incidence of in-hospital cardiac arrests in the paediatric population.

Even with optimal early warning scoring systems in place, it will still be necessary for professionals caring for children to have resuscitation skills. Treatment algorithms in the 2005 consensus guidelines, which are adopted by the European and UK Resuscitation Councils, were based on the best evidence available at the time.

The practical skills involved in resuscitation are best learned in workshops or scenarios and should be regularly updated. In-hospital resuscitation is provided by teams of healthcare

professionals who often only come together to provide resuscitation when a patient experiences a respiratory or cardiac arrest. For this reason, team training and team debriefs are essential to ensure optimal performance.

Scope of resuscitation

Paediatric resuscitation is a discipline that includes a number of elements:

- training of lay rescuers
- provision of a skilled ambulance service
- communication systems between the ambulance service and hospitals
- training of all healthcare professionals
- resuscitation team training
- resuscitation team deployment
- provision of equipment
- early recognition of the critically ill child
- management of a child in respiratory or cardiac arrest
- post-resuscitation management until the patient is transported to an area for definitive care
- audit of process and outcomes
- identification and consent of patients for whom resuscitation would not be beneficial.

Most trusts have a Resuscitation Services Department which coordinates these activities.

Resuscitation guidelines

The most recent adult and paediatric resuscitation guidelines were published in 2005. The guidelines are adopted by the European and UK Resuscitation Councils and are taught on the Advanced Paediatric Life Support (APLS) and European Paediatric Life Support (EPLS) courses. The consensus guidelines are based on the evidence available at the time of publication and are a widely accepted view on safe and effective resuscitation. They are subject to revision as new information becomes available and are fully revised every few years.

Standards for training in paediatric resuscitation

All frontline healthcare professionals should have annual training in basic life support; those who look after children are required to have training in paediatric life support.

All paediatric trainees are required to have an advanced paediatric life support certificate, either from the Advanced Life Support Group (ALSG) or Resuscitation Council (UK), and a neonatal life support certificate before appointment to paediatric registrar training.

Basic life support

The aim of providing basic life support is to maintain the oxygen supply to the tissues in the event of cardiorespiratory arrest.

On initial suspicion the child has collapsed, the rescuer should call for help and approach with care. In hospital the call for help is usually made by pulling the emergency buzzer above the patient's bed. The approach with care is important in all environments: during resuscitation in hospital, physical hazards such

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as sharps and defibrillation may pose a threat to the unwary healthcare professional.

The initial action is to establish if the child is responsive. If unresponsive, the rescuer should open the airway by performing a head tilt, chin lift manoeuvre. An infant's head is maintained in the neutral position with the head tilt into extension being used after 1 year of age. A check for the presence of breathing is made by looking at the chest and listening and feeling for breathing at the mouth.

Breathing

If the child is not breathing the rescuer must give five rescue breaths. If the rescuer has no equipment, mouth-to-mouth ventilation is used but in the hospital environment rescue breaths are given as bag-valve-mask ventilation with high-flow oxygen. The rescue breaths are given with an inspiratory time of around 1 s at the lowest pressure which will inflate the lungs so that the chest rises with a normal tidal volume. Five breaths are given over about 10 s.

Circulation

The circulation is checked by taking a central pulse and assessing for signs of circulation, such as spontaneous movement. This assessment should take 10 s. Lay rescuers are no longer taught to take a pulse but to commence chest compressions directly after the initial five rescue breaths.

In a baby under 1 year of age, the brachial or femoral pulse should be taken; in a child over 1 year of age, the carotid pulse should be taken. If no pulse is present or the pulse rate is less than 60/min in an unconscious, shocked child, chest compressions should be commenced.

Hand position for chest compressions

The recommended hand position is in the middle of the chest on the sternum, one to two finger breadths above the xiphisternum. This landmark is easily identified by lay rescuers and healthcare workers. Compression with incorrect hand position may damage abdominal organs.

Depth of compression

The chest should be compressed by about a third to a half of the original anteroposterior diameter of the chest. Compressions that are not deep enough will fail to generate cardiac output. Optimal cardiac compressions generates a cardiac output of about 20% of the patient's normal cardiac output. The chest should return to normal diameter during the relaxation phase, allowing adequate filling of the heart, which is then emptied with the next compression.

Rate of compression

The time of compression and relaxation should be equal to allow both ejection and filling of the heart. During basic life support, compressions and ventilation must be synchronized using a ratio of 15 compressions:2 ventilations. The recommended rate of compressions is 100/min; however, 100 compressions are not achieved in the minute because of the pauses to allow ventilation.

Quality of cardiopulmonary resuscitation

Cardiopulmonary resuscitation must be done well and consistently if patient outcomes are to be optimized. To this end, there

are commercially available electronic devices which may be used to monitor and give audible feedback on the rate and effectiveness of both ventilation and cardiac compressions. These devices are only designed for adults and, as yet, no device exists to monitor the quality of basic life support during paediatric cardiac arrest.

Cardiac compressions quickly cause fatigue; therefore the rescuer providing compressions should be swapped every 2 min.

Calling for secondary help

In the non-hospital environment it is recommended that basic life support is continued by the solo rescuer for 1 min before telephoning for an ambulance. If a second rescuer is available, the call to the emergency services should be made sooner.

In the hospital environment, the resuscitation team should be summoned by dialling 2222. This is the universal number for activating the resuscitation team in UK hospitals.

Some patients may return to spontaneous circulation after a short period of basic life support. These patients should be transferred to an area with appropriate monitoring and facilities for any post-resuscitation care that may be necessary.

Patients who do not have a rapid return of spontaneous circulation move seamlessly to advanced life support with the arrival of the resuscitation team.

Advanced life support

Advanced life support is built on the foundation of ongoing effective basic life support to maintain the oxygen supply to the tissues in the event of cardiorespiratory arrest. Advanced life support targets the cause of the collapse and provides specific therapy to aid the return of spontaneous circulation.

Rhythm recognition

Rhythm recognition is a vital first task to ensure appropriate advanced life support. The rhythm may be shockable or non-shockable and appropriate identification requires monitoring of the electrocardiograph (ECG). This is achieved using the defibrillator paddles or three-lead ECG. Cardiac arrest in children is rarely due to a rhythm disturbance. Pulseless electrical activity and asystole are more common during cardiac arrest in children.

Non-shockable rhythms

The non-shockable rhythms are asystole and pulseless electrical activity. Asystole is recognized on ECG as a rhythm without any ventricular activity, although P waves may be present. Pulseless electrical activity exists when the ECG shows electrical activity that should produce a pulse but no pulse is felt. Achieving return of spontaneous circulation requires ongoing basic life support, with advanced life support aimed at reversing the cause of the cardiac arrest.

The treatment of asystole and pulseless electrical activity is to provide basic life support and advanced life support aimed at correcting any reversible cause of the cardiac arrest. Adrenaline (epinephrine) is administered via the intravenous (IV) or intraosseous (IO) route ($10 \mu\text{g/kg} = 0.1 \text{ ml/kg}$ of 1 in 10 000 every 3–5 min). There are no human data to show adrenaline improves the long-term outcome of cardiac arrest. In physiological terms, adrenaline has theoretical advantages; it produces vasoconstriction which increases coronary and cerebral perfusion pressure.

When the patient is intubated, compressions and ventilation can be carried out without interrupting compressions. Ventilation should be timed for inspiration to occur during the relaxation phase in compression, allowing tidal volume to be delivered at a lower pressure.

The rate of ventilation for a child should be 12–20/min. Hyperventilation of an intubated child may easily occur during cardiopulmonary resuscitation. This can have detrimental effects, specifically vasoconstriction in the cerebral circulation; therefore, care should be taken to avoid hyperventilation. Some common reversible causes of cardiac arrest are contained in the mnemonic 4Hs and 4Ts:

- Hypoxia
- Hypovolaemia
- Hypothermia
- Hyperkalaemia (or other metabolic derangement)
- Tension
- Tamponade
- Toxins
- Thromboembolic.

These reversible causes have to be actively sought and treated or excluded. Hypoxia is reversed by ventilation with high-flow oxygen. Ventilation using a bag–valve–mask is carried out until preparation is made for intubation by an appropriately trained person.

If the patient has a history consistent with hypovolaemia, rapid infusion of a volume expander is administered to restore intravascular volume. Hypothermia is diagnosed using a low reading thermometer. Treatment is supportive with active measures used for warming. Hyperkalaemia and other metabolic derangement are diagnosed by biochemical investigation. Point of care testing for blood gas and electrolytes allows detection of metabolic derangements which, if found, should be reversed.

Tension pneumothorax should be detected by clinical examination. Cardiac tamponade usually occurs in the setting of thoracic trauma. Toxins may be suggested from the history and are detected by blood or urine analysis. Arrhythmias caused by tricyclic antidepressant overdose may respond to alkalinization of the blood. Thromboembolic disease is rare in children. A suggestive history in adults is treated with thrombolytic drugs.

Shockable rhythms

Ventricular fibrillation (VF) and pulseless ventricular tachycardia are treated by defibrillation at 4 J/kg. If the exact value is not available, the energy chosen is rounded up to the next energy level that is available. A single shock is administered every 2 min. Stacked shocks in sequences of three are no longer used.

Occasionally the nature of the rhythm is in doubt; asystole and fine VF are sometimes hard to differentiate. Current guidelines state that time should not be spent trying to defibrillate when this doubt exists, as fine VF is unlikely to convert to sinus rhythm with cardioversion. Cardiac compressions are more likely to turn fine VF into coarse VF, which is more likely to convert on subsequent defibrillation.

Biphasic versus monophasic defibrillators

Modern biphasic defibrillators have the advantage of a lower energy required for successful defibrillation with a higher success rate of cardioversion with the first shock. The standard

energy used for defibrillation in VF is 4 J/kg in both monophasic and biphasic defibrillation. Energy levels are no longer increased after the initial shock.

Safe defibrillation

The safety of the entire resuscitation team is dependent on defibrillation being carried out in a safe manner.

Automated external defibrillators

In children over the age of 8 years, an automated external defibrillator may be used on standard adult settings. Between the ages of 1 and 8 years, attenuated shock energy should be given using a paediatric programme or purpose-made paediatric pads. There is no evidence for or against the use of automated external defibrillators under the age of 1 year.

Drugs used during cardiac arrest

Adrenaline (epinephrine)

The standard dose of adrenaline during cardiac arrest is 10 µg/kg (0.1 ml/kg 1 in 10 000). This is given via the IV or IO route, followed by an IV flush. The use of high-dose adrenaline (100 µg/kg) is no longer recommended as it has been associated with a poorer neurological outcome and is particularly contraindicated in hypoxic cardiac arrest. High-dose adrenaline is reserved for exceptional circumstances, e.g. beta-blocker overdose. In the absence of other vascular access, rarely adrenaline must be administered via the intratracheal route; the dose of adrenaline is 10 times larger if this route has to be used.

There is no randomized controlled trial in humans to support or refute the use of adrenaline during cardiac arrest. Adrenaline acts as an alpha-1-agonist causing vasoconstriction and therefore it increases the coronary and cerebral perfusion pressure. Adrenaline is administered every 3–5 min during resuscitation in both shockable and non-shockable rhythms. It is therefore given during every other 2-min cycle.

Amiodarone

Amiodarone is an antiarrhythmic which acts as a membrane stabilizer. It increases the duration of the action potential and the absolute and relative refractory periods. In doing so, it reduces the likelihood of circus currents which cause many arrhythmias.

The dose of amiodarone during VF arrest is 5 mg/kg and it is flushed with 5% dextrose. Amiodarone is given immediately before the fourth shock in the VF algorithm. It can cause profound hypotension if given quickly; however, in the arrest situation the priority is to terminate VF. In the non-arrest situation, amiodarone is given by infusion rather than fast IV bolus.

Post-resuscitation care

The aims of post-resuscitation care are to optimize oxygen delivery and to prevent secondary damage. The priorities are sequenced in the 'ABC' algorithm, with respiratory and cardiovascular support given as necessary.

In the adult population, hypothermia is used to optimize neurological outcome after cardiac arrest. Studies show benefit after

arrests due to VF when the patient does not regain consciousness immediately after resuscitation. The aetiology of cardiac arrest is different in children and there is no definitive study on the effect of hypothermia in the paediatric population. Some clinicians extrapolate from the adult data and use hypothermia selectively in children.

Communication systems

The standard telephone number for summoning the resuscitation team in hospital is 2222. The communication system involves the hospital switchboard summoning the resuscitation team through a voiceover paging system. The system must be checked regularly, with daily checks of the pager system to ensure all members of the team can be contacted in an emergency.

Resuscitation team

The membership of the paediatric resuscitation team varies from hospital to hospital, but the following roles should be considered an absolute minimum:

- team leader
- airway management clinician
- dedicated trained assistant for airway management clinician
- chest compressions
- vascular access and drug administration
- scribe
- runner.

The team works best with a leader who directs the team but does not get involved in the completion of tasks. In most hospitals, the team leader will be a middle-grade paediatrician or senior nurse. There must be an experienced clinician to manage the airway; this role is usually filled by the on-call anaesthetist or intensivist.

Team training

Resuscitation courses are very useful in acquiring and practising the skills required for resuscitation of a child. However, the resuscitation team should train as a team in practice scenarios. Many hospitals now carry out this type of training and there is evidence to show it enhances team performance.

Resuscitation equipment

The Resuscitation Council (UK) gives a list of suggested equipment for paediatric resuscitation. This should be considered a minimum standard and items added to adapt to local need. A full range of sizes of all resuscitation equipment should be immediately available in all paediatric clinical areas. The Broselow system groups equipment by size and provides a convenient way of storing equipment. It tends to be used in clinical areas where paediatric resuscitation is an infrequent event.

Equipment should be checked on a daily basis and omissions corrected; a clear line of responsibility and audit trail should exist for resuscitation equipment.

Oxygen

High-flow oxygen (15 L/min) is used during resuscitation. Care must be taken to avoid depletion of oxygen when cylinders are used.

Bag-valve-mask

A self-inflating bag is the first choice for resuscitation. The advantage over an anaesthetic breathing circuit is that it may be used without a supply of oxygen, allowing ventilation with room air. The bag is used for positive pressure ventilation by squeezing an appropriate tidal volume through a mask or endotracheal tube into the lungs. High-flow oxygen and a reservoir bag allow high oxygen concentrations to be delivered.

The bag should not be used for spontaneous respiration as the inspiratory valve and rigid nature of the bag provide a high inspiratory resistance. If spontaneous respiration or continuous positive airway pressure is required, an anaesthetic breathing circuit should be used by someone trained in its use.

Endotracheal tubes

Oral intubation is used in an arrest situation. Induction of anaesthesia with drugs is not necessary in the cardiac arrest situation as the patient is already unconscious. Children in respiratory arrest may occasionally require drugs for induction of anaesthesia to abolish the cough reflex. This should only be done by an individual trained in the use of these drugs.

Traditionally, uncuffed endotracheal tubes were used in pre-pubertal children to prevent airway damage. Low pressure cuffed endotracheal tubes now come in the smallest paediatric sizes and have been used safely in small babies. Cuffed tubes prevent hypoventilation caused by large leaks.

There are a number of formulae for the size of the endotracheal tube. The author's own preference is:

$$\text{Internal diameter of tube (mm)} = [\text{Age (years)}/4] + 4.5$$

Intraosseous needles

In an emergency, IV access is usually difficult to obtain in a small child. If the child already has IV access, this should be used for the administration of drugs used during resuscitation. In situations where the child has no IV access, rapid vascular access may be gained by the insertion of an IO needle. IO needles come in a variety of sizes, although many hospitals only stock the 18 G size. IO needles may be either smooth ended or have a screw thread, and may have an end or side holes.

Insertion of an IO needle is taught on resuscitation courses in the UK. However, there is a learning curve when inserting them in children rather than manikins. Care should be taken to identify the surface of bone and a careful steady pressure with screwing action should be used until a loss of resistance is felt. The most common insertion area is in the upper tibia below the growth plate. There are also devices available which use a type of rivet gun for automatic insertion to the appropriate depth. Some of these devices may also be used in adults.

Drugs, fluids and blood products can be administered via an IO needle. The most common complication is extravasation and care needs to be taken to observe for this. Rarer complications include damage to the growth plate and infection. An IO needle may be used for up to 24 h pending more definitive IV access.

Audit

Unexpected cardiac arrest should be viewed as a serious untoward incident in the paediatric population. Each arrest should be

investigated for the cause and a thorough evaluation of avoidable factors carried out. The aim should be to avoid all cardiac arrests through earlier recognition of the sick child.

The process and outcome of resuscitation from cardiovascular collapse should be audited and regularly reviewed by the Hospital Resuscitation Committee. The standard format for data collection has been agreed internationally and is termed the Utstein style reporting template.

Stopping resuscitation

Resuscitation attempts are stopped when there is a return of spontaneous circulation. Post-resuscitation care treatment algorithms are based on the 'ABC D' priorities of optimizing oxygen delivery and preventing secondary insults.

When resuscitation attempts are unsuccessful, the decision to stop resuscitation attempts should be taken by the team leader in collaboration with the resuscitation team. The decision to stop should be made on the basis of history, response to treatment and length of time resuscitation efforts have continued.

When resuscitation attempts are stopped, careful evaluation of the patient must take place, looking for signs of life. A weak pulse or respiratory effort may be overlooked during the resuscitation attempt. If there are signs of life, post-resuscitation care may be instituted.

Witnessed resuscitation

Many parents want to be with their child during resuscitation attempts. They may wish to support the child and ensure that 'everything is being done'. Parents need to be supported by a dedicated team member during and after the resuscitation attempt. If the resuscitation attempt is not successful, the decision to stop lies with the team leader rather than the parents.

A parent should not be made to feel guilty if their decision is not to be present but should be supported by a dedicated member of staff in their decision.

Do not attempt resuscitation order

In some circumstances, as a child's life approaches a natural end, it may be inappropriate to attempt resuscitation. Each set of circumstances is unique and should be fully discussed with the family. Where it is decided that resuscitation in the event of cardiac or respiratory arrest is not appropriate, a 'do not attempt resuscitation order' is documented. This order should be subject to regular review, usually every 48 h in hospital.

Limitation of treatment agreement

For some patients with a life-limiting illness a 'do not attempt resuscitation order' does not cover all the possible options. For example, the palliative care plan may include treatment such as suction, oxygen and bag-valve-mask ventilation, while excluding intubation and cardiac compressions. For many years paediatricians have provided palliative care which has included such limits to treatment.

The Paediatric Intensive Care Society is in the process of developing the Limitation of Treatment Agreement (LOTA). This formalizes the plans made with families with respect to the aspects of therapy that are considered beneficial, including a clear written agreement of the palliative care package.

Resuscitation using extracorporeal membrane oxygenation

A small number of patients worldwide have been placed on extracorporeal membrane oxygenation (ECMO) during resuscitation for cardiac arrest. ECMO was first used for rewarming during cardiac arrest in hypothermic patients. Its use has been extended to other cardiac arrest patients for whom it is believed there is reversible pathology causing the arrest and a chance of neurological recovery. This strategy, termed ECPR, requires rapid deployment for success and is not routinely offered in most UK paediatric intensive care units. ◆

FURTHER READING

International Liaison Committee on Resuscitation. The International Liaison Committee on Resuscitation (ILCOR) consensus on science with treatment recommendations for pediatric and neonatal patients: pediatric basic and advanced life support. *Pediatrics* 2006; **117**: e955–977.

International Liaison Committee on Resuscitation. The International Liaison Committee on Resuscitation (ILCOR) consensus on science with treatment recommendations for pediatric and neonatal patients: neonatal resuscitation. *Pediatrics* 2006; **117**: e978–988.

Practice points

- Systems for early recognition of the critically ill child should exist in all hospitals to avoid respiratory and cardiac arrests
- All frontline healthcare personnel should have annual updates on resuscitation
- Resuscitation teams should have team training to optimize team performance

Management of the multiply injured child

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Abstract

Injury is the commonest cause of death and morbidity in children and accounts for most attendances at paediatric emergency departments. Optimal management of the multiply injured child relies on anticipation and preparation, followed by a standardized, consistent and structured response from healthcare professionals. Staff must be appropriately trained and supported by a regional tertiary paediatric trauma centre. Initial management involves a primary survey with resuscitation, using an 'ABC' approach, and treatment of life-threatening injuries as they arise. The details of this are outlined in this review, highlighting important child-specific factors. Once stabilized, injured children must be assessed by secondary survey to rule out all possible injuries and, if necessary, transferred to an appropriate tertiary unit. Support from regionalized tertiary centres and ongoing training for staff is paramount in optimizing outcome of the multiply injured child.

Keywords children; injury; primary survey; regionalization; resuscitation; secondary survey; training; trauma

Impact of injury in children

Injury is the commonest cause of death and morbidity in children. Globally, over 700 000 children under 15 years die because of accidental injury.¹ In the UK in 2006, approximately 300 children died from and over 2 million attended hospital because of accidental injury,² accounting for 70–80% of paediatric emergency department (PED) attendances.³ The number of children presenting with injuries increases with age,⁴ with the exception of head injuries which are commoner in the 0–5-year age group⁴ and account for over 50% of injuries sustained in those under 1 year.⁵ This correlates with a relatively high incidence of falls in those younger than 5 years, approximately 60% of accidents in this age group.^{5,6}

Falls are the commonest cause of non-fatal accidental injuries, leading to 390 000 PED attendances in those younger than 15 years in 2006.² Road traffic accidents (RTAs) are the greatest killer, responsible for half of deaths from accidental injury in

the UK in children in 2006² and approximately 12% of all child deaths in those aged 5–14 years.² The incidence of RTA injuries increases with age.^{1,7} Similar demographics have been demonstrated worldwide.^{7–9}

Thanks to successful injury prevention measures, the number of injuries has decreased over the past 10 years; in 1997 in the UK, 2.5 million children attended emergency departments with injuries and 2.01 million in 2002.² Deaths from injuries have also declined, but socioeconomic inequalities have increased. Death is twice as likely in social classes with non-professional jobs compared to those with professional occupations, and are 13 times more likely in unemployed families.⁶

One to 2% of children in the UK are abused.¹⁰ It is important to be suspicious of non-accidental injury in children, particularly those with significant injuries such as fractures that appear to be implausible given the child's developmental age or the history of mechanism given.

Minimizing the impact

Optimal management of the multiply injured child relies on anticipation and preparation followed by a standardized, consistent and structured response by healthcare professionals.

In the late 1970s the poor response to a tragic accident spurred an orthopaedic surgeon and colleagues to strive to improve and standardize management of critically ill and injured patients, with the aim of improving their outcome. So was born a course to train healthcare professionals – Advanced Trauma Life Support (ATLS®).¹¹ It has become the internationally recognized standard for the management of serious injury and has improved outcome in trauma.^{12–14} It has become a mandatory part of training for some specialities, with its importance widely acknowledged for all healthcare professionals involved in trauma care.¹⁴ Paediatric trauma poses different challenges from adult trauma and these are covered in ATLS® and subsequently developed courses such as Advanced Paediatric Life Support (APLS), Paediatric Advanced Life Support (PALS) and the European Paediatric Life Support (EPLS). They all promote a systematic approach by an organized team. The intercollegiate working party for Paediatric Emergency Medicine (PEM) services in the UK stipulates that all relevant staff in centres that deliver care to the multiply injured child should be appropriately trained.¹⁵ Thus, teams are prepared, with common language and goals, to deliver consistent and optimal care. These skills can be honed locally with regular simulator or dummy scenario training sessions in individual departments, so that when real trauma presents, responses are slick.

The structured preparation and response to the multiply injured child are outlined below. More detailed information can be obtained from the manuals for the courses mentioned above.

Preparation

As soon as the injured child is expected, prepare. The trauma team should be rallied. This team must comprise a designated team leader, an experienced anaesthetist, surgeons and other emergency department and paediatric staff. It is better that a team member is called and then leaves after the primary survey, than for there to be a delay in their attendance. The team leader

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should assign roles and take a step back to observe and coordinate the resuscitation. Equipment should be checked, although routine checks should be in place so that equipment is always ready and waiting. Most departments will have an appropriately stocked resuscitation trolley, which staff should familiarize themselves with. Drugs and fluids should be prepared. Any history given by those at the scene should alert the team to potential injuries, bearing in mind the mechanism and the different effect this may have on the child given variations in their size and relative anatomy. A car bumper, for example, may cause lower limb injuries in an older child, but significant chest or abdominal trauma in a younger child.

Children vary considerably in size and, therefore, doses of fluids and drugs, DC shock voltage and equipment size must be titrated to weight. This must be worked out quickly for the injured child, so as not to delay potentially life-saving treatment. Tools have been developed to assist the team in estimation. APLS advocate a formula based on age to give a weight in kilograms:

$$\text{Weight (kg)} = (\text{Age} + 4) \times 2$$

This is the most commonly used formula in Europe, South Africa, Australia and New Zealand.¹⁶ However, this now underestimates weight given increasing weight trends and childhood obesity.¹⁶ A proposed new formula, which has yet to be introduced, has been found to be more accurate for children aged 1–10 years:

$$\text{Weight (kg)} = (3 \times \text{Age}) + 7$$

An alternative is to use the Broselow tape, originally invented by an American family physician and based on length and weight statistics to reduce errors in estimating parameters. The tape is lined up next to the child and the child's length corresponds to colour-coded information with appropriate fluid volumes, drug doses and equipment, such as tracheal tube (TT), which are kept in matching colour-coded drawers of the resuscitation trolley. If a child is longer than the tape, adult values can be used. Although anecdotally easy to use, it is limited by availability and cost, and has also been found to underestimate the weight of today's child.¹⁷

Response

Primary survey and resuscitation

The primary survey of the child involves a rapid, sequential assessment with simultaneous management of life-threatening problems as they arise, remembering to anticipate problems at each step so they can be managed swiftly and appropriately. It follows the simple adage of 'ABC'. Regular re-evaluation, especially after an intervention is essential.

A is for Airway and Assume cervical spine injury

'First do no harm' is an invaluable principle in medical care. In a multiply injured child *always* assume that the cervical spine has been injured until it can be proved otherwise, much later on in the secondary survey. Immobilize the cervical spine using a trained person's hands with bimanual in-line technique, whereby hands are placed either side of the head and neck, keeping the

spine neutral and still. This should be their sole task until immobilization of the neck is secured with a hard collar, blocks, and chin and forehead tapes. During any necessary measures such as intubation which require these to be removed, bimanual immobilization should be used, ideally keeping the collar on.

An uncooperative child who is frightened or hypoxic and confused should not be fought with to achieve immobilization, as more harm than good may arise. Continued manual immobilization may be better tolerated or a hard collar only may have to suffice. Parental presence and reassurance of the injured child are important.

Assess the patient's airway by looking, listening and feeling. Look for any obvious obstruction and remove it if possible and safe to do so without causing further harm. Never perform a blind finger sweep. Observe chest and abdominal movement. Auscultate for breath sounds. Open the airway with positioning of the child and manoeuvres that do not compromise cervical immobilization, i.e. jaw thrust. *Remember* infants have a flat occiput and short neck, and require the neutral position to open their small, anterior airway. Padding under the shoulders may be necessary to achieve this. Young children require the sniffing position.

Give all multiply injured children high-flow oxygen, initially via a face mask with a rebreathing bag.

Use airway adjuncts if required and tolerated, such as an oropharyngeal airway. This is inserted directly as it lies in position and is not rotated as in adults. A tongue depressor can assist insertion. Avoid a nasopharyngeal airway if there is a risk of basal skull trauma or facial injuries.

If there is inadequate breathing, begin bag-valve-mask ventilation. If the airway is or is likely to become compromised, establish a definitive airway by inserting a TT as quickly and safely as possible. Indications include:

- Airway obstruction, present or impending, e.g. facial injuries, smoke inhalation or facial burns;
- Insufficient spontaneous respiratory effort;
- Ineffective respiratory effort, e.g. chest injury such as flail chest;
- Severe hypoxaemia;
- Glasgow coma score (GCS) less than 8;
- Cardiac arrest;
- Severe haemorrhagic shock.

The appropriate TT diameter in millimetres can be estimated using the formula:

$$\text{Diameter (mm)} = (\text{Age} / 4) + 4$$

Alternatively, approximate the TT diameter by comparing it to the diameter of the child's fifth finger. An uncuffed TT is often used as the conical shape of the immature airway, narrowest at the level of the cricoid ring, makes cuffed tubes unnecessary in children younger than 9 years. However, in the hospital setting, either type of TT can be used for all ages after the neonatal period without complications and the choice is therefore user dependent.¹⁸

The length in centimetres of insertion can be estimated using the formula:

$$\text{Length (cm)} = (\text{Age} / 2) + 12$$

If the nasal route is used (normally by an experienced team member and contraindicated if there is a risk of basal skull injuries), length estimates to:

$$\text{Length (cm)} = (\text{Age}/2) + 15$$

Remember that children have a relatively short trachea, so beware intubating the right main bronchus. The anatomical 'pitfalls' in the intubation of children are listed in [Table 1](#).

Check the TT position by looking at the chest wall movement and auscultating the chest for equal bilateral breath sounds. Order a chest X-ray to confirm position.

B is for Breathing and ventilation

Evaluate the effort, efficacy and effect of breathing. *Look* for signs of respiratory distress: rate ([Table 2](#)), recession and accessory muscle use. Observe chest expansion and abdominal movements. *Listen* for grunting, stridor, noisy breathing; auscultate breath sounds. *Feel* for crepitus and percuss for hyper/hyporesonance. Note also secondary effects on heart rate ([Table 2](#)), skin colour and mental status.

Anticipate the potential injuries that may be impeding breathing and treat those that are life-threatening as they are found. *Remember* children have elastic tissue. Significant forces may not fracture ribs and major internal trauma may show little external evidence on inspection. Finding rib fractures, particularly flail chest, signifies that substantially large forces have been involved in the injury, making serious internal damage very likely. Be vigilant for decompensation in these children.

Remember also iatrogenic factors may affect breathing. Aero-phagia from resuscitation or excessive crying can cause diaphragmatic splinting and impede ventilation. Pass a naso/orogastric tube to aspirate excess air. Always remember to consider the position of the TT, which may dislodge if too high or ventilate only the right lung if too low. Assess the child clinically and perform a chest X-ray.

The following chest injuries are life-threatening and require immediate treatment:

- Tension pneumothorax;
- Massive haemothorax;
- Flail chest;
- Open pneumothorax;
- Cardiac tamponade.

C is for Circulation and haemorrhage Control

Look at the skin colour. Is it poorly perfused, pale and mottled? Assess capillary refill time (CRT) by pressing firmly on the

sternum with a finger for 5 s; the skin will blanch. Release and count the time in seconds for colour to return to that of the surrounding area. In a well child this will take less than 3 s.

Check pulse rate and volume, and respiratory rate ([Table 2](#)).

Observe mental status. A decreased level of consciousness reflects poor cerebral perfusion and therefore inadequate circulation. Agitation, drowsiness and increased respiratory rate without recession also occur secondary to metabolic acidosis from circulatory failure. Decreased blood pressure (BP) and urine output (UO) are late signs in children; a UO of less than 1 ml/kg/h in children and less than 2 ml/kg/h in infants are worrying.

Remember children have a high physiological reserve, compensating for hypovolaemic shock by increasing their heart rate, systemic vascular resistance and venous tone. BP is maintained until they have lost approximately 30% of their blood volume.¹⁹ Falling BP signifies decompensating shock and is a late, pre-terminal event. CRT is a much more valuable tool than BP in assessing circulation in children.

Insert two large-bore intravenous (IV) cannulae. If unsuccessful after three attempts or 90 s, proceed to the intraosseous (IO) route. Peripheral venous cut down techniques can be resorted to if IV or IO attempts are unsuccessful.

IO needles are inserted medially into the tibia of an uninjured limb, 2–3 cm below the tibial tuberosity. Traditional needles use a screwing and pushing technique. The recently developed bone injection gun (BIG) has been shown to be similarly successful in achieving IO access, but is anecdotally reported to be easier to use,²⁰ which may have implications for achieving access, particularly in the pre-hospital setting.

Look for any obvious external source of bleeding. Apply pressure to stop it. Anticipate occult internal losses in the abdomen, pelvis, chest and long bone fractures. Stabilize any fractures by reduction and splinting of limbs or splint pelvis. 'Springing' the pelvis to test stability is no longer recommended. A surgeon should already be present as part of the rallied team, but surgical assessment is paramount once a fluid volume of 40 ml/kg has been required for resuscitation.²¹ *Remember* a surgical injury increases the risk of death six-fold in a seriously injured child and the need for surgical intervention further doubles this risk, making surgical pathology the major determinant of outcome in paediatric trauma.²² *Get a surgical opinion early.*

There are few studies of fluid resuscitation in children to guide optimal volume for fluid resuscitation. Extrapolating from evidence from adult studies involving haemorrhage, current recommended practice is to give aliquots of 10 ml/kg with careful monitoring of response.²¹ Ambulance services advocate the use of 5 ml/kg in the pre-hospital trauma setting.²³

Fluid type also raises debate. There is insufficient evidence to advocate use of colloid over crystalloid in paediatric resuscitation.^{18,24} The recommended type is 0.9% normal saline. However, if 40 ml/kg has been administered and the child remains unstable, blood products should be given thereafter.

D is for Disability

Assess the child's mental status using AVPU:

- Alert
- Responsive to Voice
- Responsive to Pain
- Unresponsive

Anatomical pitfalls in the intubation of children

- Short neck supporting a relatively large head
- Relatively large tongue and potentially large tonsils or adenoids
- Small anterior larynx
- Conical shaped airway
- Short trachea

Table 1

Age variable parameters

Age (years)	Respiratory rate (breaths/min)	Heart rate (beats/min)	Systolic blood pressure (mmHg)
<1	30–40	110–160	70–90
1–2	25–35	100–150	80–95
2–5	25–30	95–140	80–100
5–12	20–25	80–120	90–110
>12	15–20	60–100	100–120

Table 2

When a more detailed assessment is possible, the modified GCS can be used (Table 3). P, meaning only responding to pain, on the AVPU scale correlates to a score of 8 or less on the GCS.

Assess also for pupil inequalities and lateralizing signs. Worrying features associated with a history of head injury necessitate urgent neuroimaging and neurosurgical input. Prevent secondary brain injury by optimizing oxygenation, cerebral perfusion and therefore systemic perfusion. Consider hypertonic saline to lower intracranial pressure if indicated. Treat any fits promptly. Remember altered mental status, such as confusion, agitation and decreased consciousness, also occurs if the child is hypoxic or hypoperfused, reiterating the importance of optimal management of 'ABC'. Also, *never* forget to give glucose in any seriously ill child with an altered level of consciousness, and treat any hypoglycaemia promptly.

E is for Exposure and Environment

While it is important to undress the child to inspect them fully for multiple injuries, remember it is vital to keep them warm. Hypothermia can cause vasoconstriction, acidosis and consumptive

coagulopathy,²⁵ impeding resuscitation. A child's high surface area to body mass ratio makes them more prone to losing heat and this must be compensated for by covering them after each examination and having a warm resuscitation room and warmed fluids.

Constant re-evaluation and assessment throughout is paramount, particularly after any intervention.

Pain control

Pain control is important in trauma but should be carefully monitored and titrated to the child's response and level of consciousness. The drug of choice is IV morphine at 0.1–0.2 mg/kg, with lower doses given if child shows decreased consciousness. Entonox may also be used but is contraindicated if there is a pneumothorax or basal skull fracture.

Secondary survey

Once life-threatening issues have been dealt with and the child is more stable, a secondary survey should be performed. This is

Modified Glasgow coma score (GCS) for children and for infants and small children**Modified GCS for children****Eye opening:**

Spontaneous	4
To voice	3
To pain	2
No verbal response to pain	1

Best motor response:

Obeys verbal command	6
Localizes to pain	5
Withdraws from pain	4
Abnormal flexion to pain	3
Abnormal extension to pain	2
No verbal response to pain	1

Best verbal response:

Orientated, appropriate	5
Confused	4
Inappropriate words	3
Incomprehensible sounds	2
No verbal response to pain	1

Modified GCS for infants and small children**Eye opening:**

Spontaneous	4
To voice	3
To pain	2
No verbal response to pain	1

Best motor response:

Spontaneous or obeys command	6
Localizes to pain/withdraws from touch	5
Withdraws from pain	4
Abnormal flexion to pain	3
Abnormal extension to pain	2
No verbal response to pain	1

Best verbal response:

Smiles, babbles, fixes and follows	5
Irritable cries but consolable	4
Cries to pain, persistently irritable	3
Moans to pain, agitated, restless	2
No verbal response	1

Table 3

a detailed head-to-toe assessment to identify any other injuries. Thirty to 45% of children with trauma have multiple injuries and at least one fracture.²⁶ A careful history should be taken from the child, if possible, paramedics, bystanders and family members. Consider carefully the mechanism of injury to anticipate possible injuries.

Systematically examine:

- Surfaces, head-to-toe, front and back;
- Orifices, mouth, nose, ears, orbits, rectum, genitals;
- Cavities, chest, abdomen, pelvis, retroperitoneum;
- Extremities, all limbs.

Relevant imaging should be performed as necessary.

It is very important to document all findings so that if the child is transferred, receiving teams know the extent of any injuries.

Transfer after stabilization

Regionalized trauma networks should be in place to provide both early advice for all centres receiving the multiply injured child and facilitation of transfer to an appropriate tertiary unit.¹⁵ Shorter pre-hospital times and definitive care at a designated paediatric tertiary centre optimize outcome.^{27–32} The ideal of direct transfer from the scene to a tertiary paediatric trauma centre is often not feasible because of the shortage of such centres. However, regionalization, support and training of other units in close proximity to the injured child, followed by transfer to a tertiary unit as soon as the child is stabilized, support optimal outcome.^{29,31,32}

Parental presence

Parents should be encouraged to be present at resuscitation to reduce the child's fear by comforting them and promoting the child's cooperation with management. It is important also for parents to witness resuscitation efforts, so if unsuccessful they have an increased acceptance that everything possible was done. This has been shown to reduce long-term anxiety and depression in parents if children die.¹⁸ A member of staff should be available solely to offer support and explanation to the parents throughout the resuscitation.

Over 80% of children and their parents elicit some symptoms of acute stress after accidental injury.³³ At least 10% develop acute stress disorder³⁴ and 13–45% of injured children are found to have post-traumatic stress disorder (PTSD) later on.³⁵ Once the child is physically well, explaining that initial distress symptoms are to be expected and how to deal with them can allay anxiety, but screening tools should be in place to identify those children and parents at risk of PTSD so appropriate follow-up can decrease subsequent morbidity.^{33,36}

It is important that the resuscitation team also has a chance to debrief and to raise questions and concerns, and that all staff have access to appropriate support if they have found a particular case distressing. ♦

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Practice points

- Be prepared, keep up to date with relevant training and information
- Be systematic and structured in your approach to the multiply injured child
- Be a team player. Ensure all key staff are present and prepared. Communicate well with each other and the regional network
- Be keen to improve. Practise scenarios regularly in your department in anticipation of the real event. Audit your team's responses locally and participate in national audit
- In the UK, register with the Trauma Audit and Research Network (TARN) where appropriate³⁷

Management of apparent life-threatening events

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Abstract

Apparent life-threatening events in infancy (ALTE) present a common yet complex management problem for the clinician. While an ALTE generally represents a benign event, in rarer instances it may indicate a serious underlying disorder. In most circumstances patients will require admission for a short period, thus providing the opportunity to perform a systematic, thorough examination, followed by the selective use of investigations. In all situations, however, even those with an unambiguous diagnosis, follow-up must be provided to detect recurrent episodes and to monitor long-term sequelae.

Keywords apparent life-threatening event; ALTE; apnoea of infancy; infantile apnoea

An apparent life-threatening event (ALTE) was defined in 1986 by the National Institutes of Health (NIH) Consensus Development Conference on Infantile Apnoea and Home Monitoring. It is 'an episode that is frightening to the observer and that is characterized by some combination of apnoea (central or occasionally obstructive), colour change (usually cyanotic or pallid but occasionally erythematous or plethoric), marked change in muscle tone (usually marked limpness), choking or gagging. In some cases the observer fears that the infant has died.'¹ An ALTE refers not to a specific diagnosis, therefore, but to a description of an array of symptoms.

The management of an ALTE presents three significant challenges for the clinician. First, the child is often asymptomatic at presentation, leading to reliance on the caregiver's recall which, given the traumatic nature of the precipitating event, can vary in accuracy. Second, while it is most likely that an ALTE represents a benign event, it can also signify a more serious illness. The dilemma for the clinician lies in differentiating these mild events, such as a simple choking spell, from the more serious illness such as bacterial sepsis. Third, the extensive range of potential causes often results in a correspondingly lengthy set of investigations. While some investigations are clearly indicated,

less targeted testing is unlikely to unearth a causal factor² and also runs the risk of obtaining false-positive results.

These challenges are underscored by the difficulties associated with researching this disorder. As there is no specific discharge code for ALTEs, retrospective studies have been forced to depend on proxy classifications such as cyanosis or apnoea. Prospective studies are equally problematic as the definition is extremely broad, encompassing both mild physiological disturbances and pathological symptoms. As a result, research has focused on those patients who have been referred to specialty services, leading to an inflated emphasis on single-system causes. The resulting lack of an evidence-base or systematic approach can lead to wide variations in the clinical care of ALTEs. These variations relate most specifically to the use of diagnostic tests, medications, length of stay and costs.³

Epidemiology

The precise incidence of ALTEs is difficult to determine due to the broad range of definitions used by researchers and the lack of complete population-based studies. An ALTE can occur between 1 week and 11 months of age, with a peak incidence around 2 months.³⁻⁸ One prospective study over 2 years, covering almost 40% of all births in Sweden, suggested an incidence of 0.46/1000 live births.⁹ While these infants experienced a short apnoeic episode ('attack of lifelessness'), no medical cause was determined at the time. In infants with apnoeic episodes requiring basic resuscitation, an incidence of 0.9/1000 live births was reported.¹⁰ Using the criteria established by the NIH consensus definition, others have described ALTEs as occurring in 0.6–0.8% of all emergency department visits for infants younger than 1 year old,^{4,9} and ranging from 0.6 to 2.46/1000 of liveborn infants.^{5,11}

Description

The key issue in identifying an ALTE lies in differentiating between normal physiology and a pathological event in each of the NIH's consensus statement's four components of apnoea, colour change, muscle tone and choking or gagging.

Apnoea refers to a complete cessation of respiratory air flow. Physiological apnoea is a normal phenomenon in young infants with one study reporting that 43% of healthy term infants experienced a respiratory pause lasting up to 20 s during a 3 month period.¹² During these apnoeic spells there is no evidence of physiological disturbance such as bradycardia, cyanosis or change in muscle tone (usually reduced). Physiological apnoeic spells do not appear to be more common in infants with a previous history either of ALTE or of sudden infant death syndrome (SIDS) in a sibling.¹²

In contrast, however, pathological apnoeic spells consistently result in a degree of physiological disturbance. The degree of cyanosis, bradycardia or hypotonia depends to a large extent on the length of the apnoeic event. Pathological apnoea can be due either to obstructive or central causes. Obstructive apnoea is defined as partial or total occlusion of the airway. This leads to choking or gagging movements with ineffectual breathing movements in addition to the physiological disturbance. Central apnoea is caused by a decreased respiratory drive from the

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brain, leading to very shallow or absent breathing movements. If obstructive apnoeas persist, then central apnoeic depression will supervene eventually. If no cause for this is found in an infant of more than 37 weeks' gestational age, it is referred to as apnoea of infancy. This can be distinguished from apnoea of prematurity which occurs in infants up to 37 weeks' gestational age.

The colour change of most concern is central cyanosis. This is due to the presence of more than 5 g/dl of unsaturated haemoglobin in the blood and is manifested by a blue appearance to the lips and tongue. It occurs if there is inadequate oxygenation and results from prolonged apnoea. Central cyanosis can be normal in young infants during brief crying spells and may represent intracardiac shunting. Pallor or plethora may be attributable to a broad range of physical effects and, if temporary, usually does not indicate a serious pathological process.

Muscle tone changes consist of limpness, increased tone or twitching. Limpness or hypotonic spells can accompany apnoea and represent a central neurological dysfunction. Increased tone or twitching may result from a choking episode or seizure and is suggestive of neurological dysfunction. Choking or gagging implies a response to partial or complete (usually upper) airway obstruction. It is normal in young infants during a feed and generally is short-lived. Prolonged or repeated episodes may signify swallowing or anatomical problems with the upper airway or digestive tract.

History

Eliciting a comprehensive history is crucial in the evaluation and management of an ALTE. Understandably, however, the unexpected and frightening nature of the event may affect the caregiver's ability to provide precise details. If possible, the history should be taken from each person who observed the infant either during or immediately after the episode.

The most salient feature in the history is whether the apnoeic spell is either central or obstructive/mixed. Determining this may direct the management of the more common causes (Table 1¹³). If the infant experienced a central apnoeic spell with colour change, then causes affecting global brain function or cerebral perfusion should be sought. These include seizure, cerebral infection, metabolic disease, cardiac dysrhythmia or septic shock. If the infant suffered an obstructive apnoeic spell or mixed obstructive/central spell, then causes associated with airway obstruction need to be investigated. Examples of these are vomiting, persistent coughing, aspiration of foreign body or non-accidental trauma.

All details surrounding the event are of potential significance. One useful approach is to consider sequentially:¹⁴

1. *Description of the event.* The event needs to be fully described, including breathing pattern, colour and change in muscle tone. Were the eyes bulging with stiffening, suggesting an airway obstruction? Were the eyes closed or rolling backwards with hypotonia, suggesting a central apnoeic event? Were there

Common causes of ALTEs and suggestive historical features (adapted from Fu and Moon¹³)

Type of event	System affected	Condition	Historical features
Central apnoeic event	Central nervous system	Seizure	Loss of consciousness Eye deviation Convulsion
		Cerebral infection (meningitis)	Fever or hypothermia Irritability or lethargy
		Metabolic disease	Feeding difficulty or frequent, severe illnesses Family history of metabolic disease
		Apnoea of infancy	Prematurity Lack of other associations
	Cardiovascular	Dysrhythmia Congenital heart disease	Feeding difficulties Sweating or dyspnoeic on feeding
	Infectious disease	UTI, sepsis	Fever or hypothermia Lethargy
Obstructive or mixed apnoeic event	Gastrointestinal	Gastro-oesophageal reflux disease	Vomiting, choking or gasping Recent feeding Milk in mouth or nostrils
	Respiratory	Infection - pneumonia, bronchiolitis, pertussis infection Aspiration Airway abnormality	Coryza, coughing, wheezing Fever or hypothermia Stridor or unusually noisy breathing
	Child maltreatment	Child abuse Factitious illness	Difficulty feeding History of trauma Blood in nose or mouth Inconsistent history Previous ALTE

Table 1

twitching movements suggestive of a seizure? How long did the event last? The duration is often only an estimate but can be described in terms of seconds or minutes.

2. *Circumstances and environment prior to the event.* Prior to the event where was the child located and in what position? Was the infant in a bed or cot, or on the sofa? Was the child's face covered with a blanket? If the child was sleeping, what caused the parent to check the child and what was observed? Had there been a recent feed? Could the child have aspirated a foreign body?
3. *Intervention to stop the event.* The intervention to interrupt the event needs to be noted. What resuscitative measures were performed and how long was it before the infant returned to normal? In general, the more aggressive the resuscitation (mouth-to-mouth instead of gentle stimulation) and the longer the time until normal alertness returns, the more detailed the investigation and observation required.
4. *Recent and family history.* A general medical and social review needs to be covered. This should include recent illness, previous history of similar events and family medical history. A review of drugs given to the infant, including over-the-counter medications or alternative medicine remedies, is important. This should also include medications present in the home (due to the risk of unintentional ingestion) or medications taken by the mother if breast feeding.

A special mention needs to be made regarding child maltreatment, which may present with few clinical signs. Research has estimated that between 2.3% and 32% of ALTEs are related to child abuse.^{6,8,15–17} The wide variation may be attributable to the differing methods of abuse detection, inception cohort, definition of abuse and length of follow-up. In one study of 471 infants presenting with ALTEs, 54 (11%) were diagnosed as having suffered abuse.⁶ However, ALTE infants with known medical causes were excluded and the abuse was detected cumulatively over a 5-year follow-up period. Two (0.4%) patients were identified at initial presentation and 17 (3.6%) within 1 year. The abuse took various forms, including physical, sexual, drug exposure, emotional maltreatment and Munchausen syndrome by proxy (or factitious illness). ALTEs may also be a presentation of non-accidental poisoning.^{18,19}

The clinician should be especially alert to several factors suggestive of maltreatment beyond external physical signs such as bruising or fractures. These include a history of recurrent ALTEs either within the family or occurring only in the presence of the same caregiver, prior SIDS victims in the family at an unusually late age, fresh blood in the nose or mouth following the ALTE, and bruising that is inconsistent with the event or resuscitation.^{15,20–22} Other researchers have suggested additional circumstances, such as a delay in seeking medical care and a history that is either confusing, varies among the caregivers or changes during the course of the evaluation.¹⁷

Examination

A complete examination needs to be performed covering the major systems affected in the differential diagnosis (see Table 2²³). Special attention should be paid to the airway and respiratory system, congenital anomalies, signs of a new illness or neurological abnormalities. The clinician should search carefully for evidence of maltreatment and document the caregiver's interaction with the infant.

Differential diagnosis (modified from DeWolfe²³)

System	Condition
Gastrointestinal (33%)	Gastro-oesophageal reflux disorder Gastroenteritis Oesophageal dysfunction Colic Surgical abdomen Dysphagia
Neurologic (15%)	Seizure Central apnoea/hypoventilation syndromes Head injury or intracerebral haemorrhage Meningitis/encephalitis Hydrocephalus/brain tumour Neuromuscular disorders Vasovagal reaction Congenital malformation of brainstem
Respiratory (11%)	Respiratory syncytial virus Pertussis Aspiration pneumonia Other lower respiratory tract infection Reactive airways disease Foreign body
Otolaryngologic (4%)	Laryngomalacia Subglottal and/or laryngeal stenosis Obstructive sleep apnoea
Cardiovascular (1%)	Congenital heart disease Cardiomyopathy Cardiac dysrhythmia Myocarditis
Metabolic/endocrine	Electrolyte disturbance Hypoglycaemia Inborn errors of metabolism
Other infections	Sepsis Urinary tract infection
Child maltreatment	Shaken baby syndrome Intentional suffocation Munchausen by proxy syndrome/factitious illness
Other	Physiological event Breath holding spell Choking Drug or toxin reaction Unintentional smothering Anaemia Hypothermia
Idiopathic apnoea of infancy (23%)	ALTE

Table 2

Differential diagnosis

As the differential diagnosis of an ALTE is extensive, a systematic approach is indicated. Several studies have attempted to rank the most likely causes.^{3,24,25} Table 2 shows the relative frequencies

of each system disorder causing an ALTE. This probabilistic approach to diagnosis is particularly useful if the infant presents with no clinical signs. It should be noted that in 23–50% of infants who experience an ALTE no cause will be found,^{5,21,24} a condition often referred to as idiopathic ALTE. This section will discuss the three most frequently identified diagnoses: gastro-oesophageal reflux disease (GORD), seizures and respiratory infections.

Gastro-oesophageal reflux disease

GORD is the most consistently identified diagnosis. The problem, however, is whether this finding is causative of the ALTE or simply a common incidental finding. It is well known that there is a high prevalence of physiological gastro-oesophageal reflux in infants. One study of 65 infants with ALTEs presenting to an emergency department detected GORD on radioisotope milk scan in 41 patients (89%).⁴ However, this result was determined subsequently to be clinically significant in only 17 infants (41%). The scan indicated the presence of GORD in 16 infants already diagnosed with other conditions, such as a urinary tract infection (UTI), seizures and pertussis. Therefore, GORD can co-exist with other diagnoses and may be over-diagnosed as a sole cause of ALTE.

Seizures

A seizure is the second most common diagnosis associated with an ALTE. One recent study of 93 infants presenting with an ALTE revealed that 19% (18 infants) had a neurological cause, the majority of which were seizures (15 infants).²⁶ Furthermore this study also found that a history of unresponsiveness followed by a change in body tone was highly predictive of an epileptic seizure. In this group, however, standard brain imaging and electroencephalography were often normal. This led the authors to conclude that detailed, repeated history and examination should remain the primary diagnostic tool.

Respiratory infections

Respiratory infections (such as rhinitis, bronchiolitis, pneumonia and pertussis) are also very common diagnoses associated with an ALTE presentation. The combination of airway secretions, coughing and breathing difficulties lead to the possibility of a temporary airway obstruction resulting in apnoea, cyanosis or choking episode. Usually the clinical symptoms and signs are obvious to the clinician, and thus treatment and investigation can be appropriately focused. In a recent study, Altman et al reviewed the records of all infants with ALTEs subsequently discovered to have an infection.²⁷ Of these infants, 84% had a respiratory infection (usually bronchiolitis), while 79.6–100% had symptoms suggestive of a respiratory tract infection, such as nasal symptoms, cough or signs of respiratory distress.

Management

Following a detailed history and examination, the clinician needs to decide on the most appropriate management of the infant. In the absence of either evidence-based guidelines or a standard minimal work-up,²¹ several authors have suggested treatment plans.^{4,13,23,24,27} Figure 1 presents a staged approach to a management plan for an ALTE in a previously healthy infant. The first decision to be taken is whether or not to admit the child.

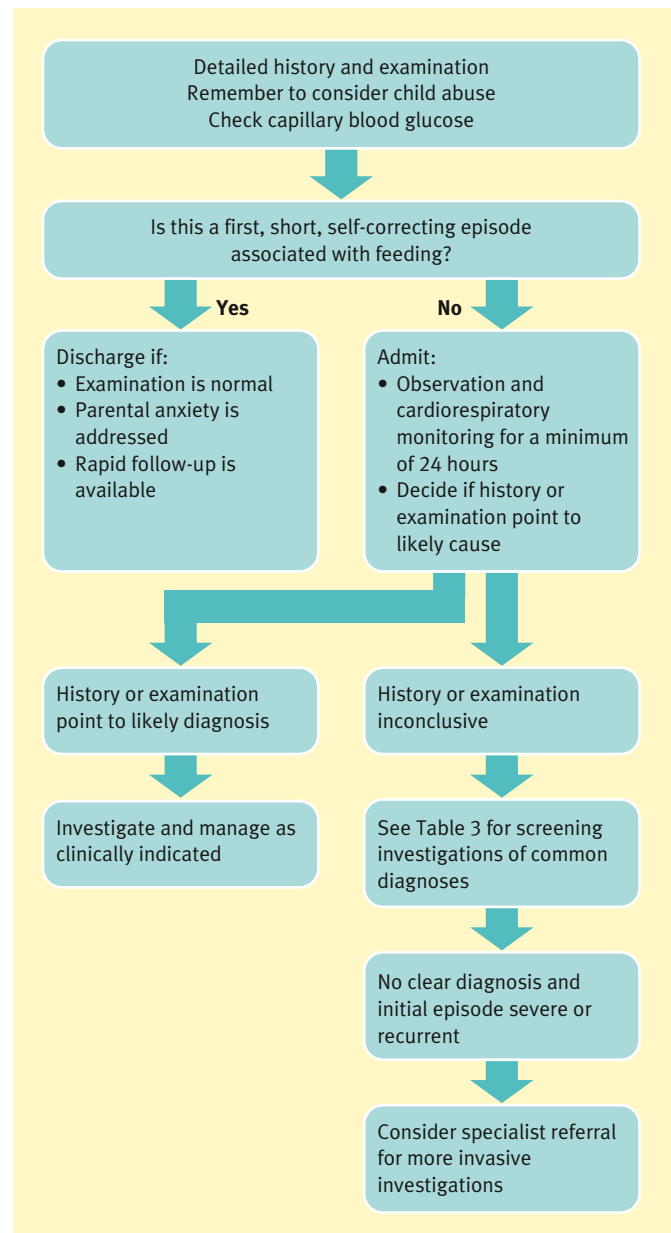


Figure 1 Suggested initial management plan for an ALTE in a previously well infant (adapted from McGovern and Smith²⁴).

If the event is a short, self-correcting episode associated with feeding (mild choking spell) and the examination (including observations and blood glucose) is normal, then the infant can be discharged. The possibility of child maltreatment should be considered and the child protection register checked. Parental anxiety should be addressed and rapid follow-up must be available. If there are any concerns at the initial assessment, however, most clinicians would admit the infant for a short period of observation.

Recently, Claudius and Keens examined criteria that would allow low-risk ALTE infants to be discharged from the emergency department.²⁸ This prospective pilot study looked at the subsequent outcome of 59 infants admitted with an ALTE. Eight infants (14%) met the criteria for high-risk ALTE (age ≤ 1 month, multiple ALTEs within 24 h), indicating an underlying problem, and were hospitalized. However, the authors note that this study was not

designed to cover rarer conditions that may present with a single ALTE, and that a larger multicentre trial would be necessary before a selective hospitalization strategy could be widely implemented.

A short period of hospitalization provides several advantages for evaluation and treatment.²³ First, the infant can be put on continuous cardiorespiratory monitoring with repeated ALTEs recorded and treated should they occur. Repeat ALTEs are significant and indicate an ongoing pathological process such as seizure or severe GORD.²⁸ Second, a range of more complex investigations can be completed in a hospital setting. Third, a period of hospitalization enables concerns about inappropriate care of the child to be addressed. Finally, specific treatment can begin and the family can be provided with education, reassurance and counselling. There is also often considerable anxiety around ALTEs and the family can be taught basic resuscitation techniques which help create confidence. The use of home apnoea monitors, while popular, is controversial as they do not prevent SIDS and may create excessive anxiety due to false alarms. Home apnoea monitors are currently recommended for selected children with a high risk of repeat apnoeas, such as those with airway problems, chronic lung disease or tracheostomy.²⁹

The duration of hospitalization will vary according to the nature and severity of the event. A Scandinavian consensus statement in 1993 advised hospitalization for up to 3 days on the basis that the risk for recurrent ALTEs within a 3-day period might be as high as 30%.³⁰ One study has evaluated the merits of either a 24- or 72-h stay in 65 infants admitted with ALTE.³¹ For 64 of the 65 patients, clinical observation and investigations revealed the cause of the ALTE within 24 h. However, one infant with no symptoms on the first day had a prolonged apnoea at 48 h, although this did not affect outcome. The ultimate prognosis for all infants was excellent, with no recurrent ALTEs and no deaths at 1 year of age.

More recent research analyzed the characteristics of 12 067 patients (aged 3 days–5 months) admitted to paediatric hospitals with ICD-9 codes compatible with an ALTE, such as apnoea, syncope, altered consciousness and cyanosis.³ Results indicated a mean length of stay of 4.4 days (standard deviation \pm 5.6 days) and a wide range of investigations. These findings highlight the authors' call for an evidence-based national standard of care for ALTE, and for research into the effect on patient outcomes of different diagnostic and management strategies.

Several researchers have developed lists of tests to cover the most likely diagnostic possibilities.^{2,4,7,16,32} In Brand et al's case series of 243 infants with ALTE, patients were divided into those with a contributory history and physical examination (70%) and those with non-suggestive initial findings (30%).² In the latter group, the study found that five tests (GORD screening, urine analysis/culture, brain neuroimaging, pneumogram and white blood cell count) were helpful in unearthing hidden causes in 46% of the patients. The remaining 54% were discharged with no diagnosis and it is possible, therefore, that there was undetected serious pathology.

Future research should focus on a large population-based prospective study to test the validity of various diagnostic strategies. In the interim, we suggest that, as a first step, investigations should be based on the admitting clinical history and examination. If there are no suggestive initial findings, then more in-depth testing is required (Table 3^{2,24,33,34}). This is especially so if the ALTE is frequent and/or severe.

Prognosis

For most infants presenting with an ALTE the prognosis is good. One study followed 65 infants who had presented with an ALTE.⁴ Over a 3-year follow-up period there were no deaths, and 88% (57) of infants had only one initial admission. The remaining 12% (8) of infants had repeated ALTEs due to significant underlying disorders. In other research the long-term developmental follow-up of children who had experienced an ALTE was examined.^{35,36} No differences were found in developmental skills or behaviour.

There have been few follow-up studies that specifically examine the long-term outcome of an ALTE. In one systematic review of 643 infants with an ALTE, five deaths were reported (0.8%).²⁴ However, comprehensive follow-up was complete in only three of eight studies, so it is possible the death rate was an underestimate. A more recent study evaluated all infants admitted to a tertiary paediatric hospital with a diagnosis broadly compatible with an ALTE.⁶ Patients found on admission to have a definitive medical problem were excluded from the study. Follow-up was continued for an average of 5.1 years. The authors reported two deaths (0.42%) due to chronic epilepsy and severe developmental delay. They also noted that 54/471 (11%) were found to be victims of child abuse and 23/471 (4.9%) had adverse neurological outcomes. There were no cases of SIDS.

Given the similar presentations of an ALTE and SIDS it is understandable that for many years the two conditions were considered to be related. Indeed older terms such as

Common diagnoses and suggested evaluation for the well infant with the first ALTE (adapted from Brand et al,² McGovern and Smith,^{24,33} Warren et al³⁴)

Diagnosis	Test or evaluation
Gastro-oesophageal reflux disease (GORD) or severe, repeated choking spells	Feeding observation, barium contrast upper gastrointestinal studies, other studies to evaluate GORD
Respiratory tract infection	Oxygen saturation, full blood picture, chest X-ray, nasal aspiration for pertussis, respiratory syncytial virus or respiratory pathogens
Seizure	EEG, brain neuroimaging, metabolic studies, video surveillance
Undifferentiated infection/sepsis	Full blood picture, blood gas, lactate, chest X-ray, lumbar puncture, urine and blood culture
Dysrhythmia/congenital heart disease	ECG, 24-h ECG, chest X-ray
Child maltreatment	Fundoscopy for retinal haemorrhages, urine toxicology, skeletal survey, neuroimaging
Apnoea	Continuous oxygen saturation, sleep study

Table 3

'near-miss sudden infant death syndrome' or 'aborted cot-death' were often used to describe an ALTE. SIDS or sudden unexplained death in infancy (SUDI) is defined as the sudden death of an infant younger than 1 year for which no cause has been found after a careful assessment of the history, autopsy and the environment.^{20,37}

SIDS cases rarely have a preceding history of an ALTE. It is likely that there is only a small overlap between SIDS and ALTE. Clear epidemiological differences exist between the two conditions.³⁸ ALTE tends to occur earlier in life than SIDS at a median age of 8 weeks compared to 18 weeks in SIDS.⁵ Also, intervention programmes have significantly reduced frequency of SIDS with no corresponding effect on the frequency of ALTEs. The age of ALTE mothers is similar to the normal population distribution, whereas SIDS mothers are disproportionately younger.⁵ Maternal smoking is the only risk factor that has been consistently noted in both ALTE and SIDS families.^{5,38}

Conclusion

In the majority of cases, an ALTE represents a benign event. However, due to the lack of clarity surrounding the event's description and the potential of a serious underlying disorder, patients often will need to be admitted. Hospitalization offers the opportunity to perform a systematic, thorough history and examination, followed by a selective use of investigations. Admission also enables medical staff to observe, educate and support parents. In all situations, however, even those with a definitive diagnosis, follow-up must be provided to detect recurrent episodes and to monitor long-term sequelae. ♦

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Practice points

- ALTEs represent common, usually benign, physiological events
- In rare instances, an ALTE may be the first presentation of a serious underlying disorder
- Most infants require a short admission to evaluate the child comprehensively and provide parental education and support
- The possibility of child maltreatment should be considered and the child protection register checked
- ALTEs have no definitive relationship to sudden infant death syndrome. In all circumstances infants should receive careful follow-up to review and assess recurrent events.

Haemofiltration therapy

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Abstract

This review provides a practical guide to haemofiltration (HF) in children. HF is used predominantly in paediatric intensive care units (PICUs) as one of the modalities of renal replacement therapy (RRT). Its use has expanded beyond the narrow scope of treatment for acute renal failure (ARF) to include fluid removal in patients with massive capillary leak, coagulopathies and also toxin removal in inborn errors of metabolism. The main advantage of using HF is to provide continuous solute clearance and fluid removal, in a controlled manner. This makes it the preferred RRT for patients with cardiovascular instability and hypotension. The basic principles of HF are similar for adults and children. Vascular access is critical and safer machines have been developed for volumetric control. However, nursing knowledge and expertise is essential and there needs to be close collaboration between PICU and nephrology staff. Randomized trials of HF treatment in children have not been undertaken but improved survival has been linked to intensity of HF and fluid removal.

Keywords acute renal failure; continuous renal replacement therapy; haemofiltration; paediatric intensive care units

Introduction

The care of a child with multiorgan system failure (MOSF) and the need for renal replacement therapy (RRT) has changed dramatically over the last 20 years.^{1,2} In the 1970s the RRT of choice was acute peritoneal dialysis (PD), especially for isolated failure of the kidney. However, the technique's low complexity is balanced against moderate efficiency. Intermittent haemodialysis (HD) was frequently used in renal units where nursing expertise was available. However, HD is not suitable in hypotensive patients, requires access to a suitable water supply and gives only moderate fluid removal in short sessions. Haemofiltration (HF) has been increasingly employed in the intensive care situation

where moderate solute removal and good volume control may be achieved even in hypotensive patients (Table 1).

Advancement and improvement in the care of critically ill children with congenital cardiac disease, and in children with sepsis, bone marrow and solid organ transplantation has led to a dramatic broadening of paediatric acute renal failure (ARF) epidemiology.^{3,4} More patients in the paediatric intensive care unit (PICU) situation require continuous renal replacement therapy (CRRT), which is now delivered by dedicated HF machines with more concise volumetric control.⁵

HF is very dependent upon the quality of the vascular access to provide adequate blood flows, as well as trained nursing staff to deliver the treatment.^{6,7} Such expertise can be developed and maintained in units remote from paediatric nephrology centres by support from an outreach service using a renal critical care educator.⁸

Historical background

In 1977 Kramer published the first report of continuous extracorporeal treatment in a patient with ARF.⁹ The femoral artery had mistakenly been punctured instead of the femoral vein. Kramer left the arterial catheter in place and was able to demonstrate that the arterial blood pressure was sufficient for a filter to achieve satisfactory filtration capacity without employing a blood pump. Owing to its surprising simplicity, this continuous arteriovenous haemofiltration (CAVH) quickly gained ground, particularly in hospitals without other facilities for treatment of ARF.

Types of haemofiltration

In general, HF may be divided into the following modalities:

1. Continuous arteriovenous haemofiltration (CAVH);
 2. Continuous veno-venous haemofiltration (CVVH);
 3. Continuous arteriovenous haemodiafiltration (CAVHDF);
 4. Continuous veno-venous haemodiafiltration (CVVHDF).
- CAVH has largely been replaced by CVVH and CVVHDF, particularly in intensive care units.¹⁰

CAVH(DF) requires both arterial and venous access. This modality offers the significant advantage of simplicity. Unlike CVVH(DF), no external pump is required for optimal CAVH(DF). However, certain optimal conditions are required for this modality to be effective, including a mean arterial blood pressure consistently above 50 mmHg and a haematocrit of 30%. In general, the paediatric and neonatal populations have a lower mean arterial blood pressure and higher haematocrit, which may decrease the usefulness of this modality in these populations, hence its use has been largely replaced by CVVH(DF).

Principles of haemofiltration

The transfer of solutes across a semi-permeable membrane may be accomplished by diffusion or convection.

Diffusion

Diffusion refers to solute movement across a semi-permeable membrane (down a concentration gradient), which results in the same concentration on either side of the membrane. Diffusion is

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Comparison of modalities of renal replacement therapy for acute renal failure

Type	Complexity	Use in hypotension	Efficiency	Volume control	Anticoagulation
Peritoneal dialysis	Low	Yes	Moderate	Moderate	No
Intermittent haemodialysis	Moderate	No	High	Moderate	Yes
CVVH	Moderate	Yes	Moderate	Good	Yes
CVVHDF	High	Yes	High	Good	Yes

CVVH, continuous veno-venous haemofiltration; CVVHDF, continuous veno-venous haemodiafiltration.

Table 1

the predominant method utilized in HD and partially in CAVHDF and CVVHDF.

Convection

Convection refers to solute movement together with solvent by means of filtration across a semi-permeable membrane in response to transmembrane pressure.¹¹ Convection is the predominant method utilized in CAVH and CVVH.

At its simplest CVVH uses convection exclusively. In this case, the ultrafiltrate produced is replaced completely or in part by a replacement fluid. Solute clearance is dependent upon blood flow rate and surface area of the membrane used. Thus, any factors which influence this condition will ultimately affect the overall efficiency of the system. HF provides better removal of large molecules (e.g. beta-2 microglobulin). CAVHDF and CVVHDF offer both convection and diffuse solute clearance with addition of dialysis fluid similar to that in HD (Figure 1). This technique may offer an improved clearance rate of some toxins and middle molecules. Again, fluid balance can be maintained

or titrated to the desired rate by administration of replacement solution. The replacement fluid can be administered either pre-membrane filter (pre-dilution) or post-membrane filter (post-dilution). Newer equipment can now perform a mix of pre- and post-dilution. Experience in paediatrics is still limited, with manufacturers suggesting mixes of 50/50 and 70/30 as a starting point for treatment.

Traditionally pre-dilution replacement is preferred for veno-venous circuits because, theoretically, blood viscosity is decreased and it may improve filter longevity as well as decreasing anticoagulant requirements. Post-dilution replacement is preferred for arteriovenous circuits and may result in improved solute clearance.

Indications

The following are indications for haemofiltration:

1. Hypervolaemic states, usually with renal insufficiency;
2. Electrolyte abnormalities;

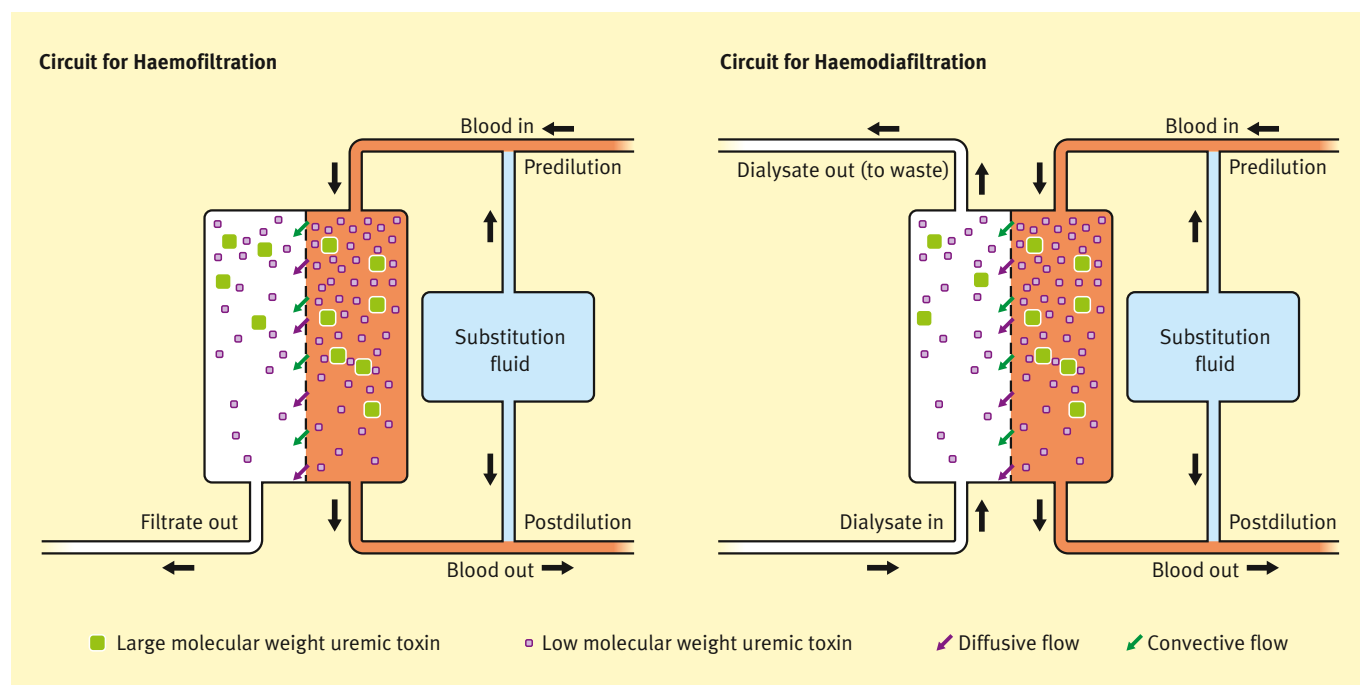


Figure 1 Circuit for (a) haemofiltration and (b) haemodiafiltration. (Reproduced with permission from Kotanko P, Kuhlmann MK, Levin NW (eds). *Comprehensive Clinical Nephrology*, 3rd edn. London: Elsevier, 2007:958.)

3. Catabolic patient with increased nutritional needs;
4. Sepsis and capillary leak syndrome;
5. Poisoning (occasionally in combination with HD);
6. Hyperammonaemia and inborn errors of metabolism;
7. Hepatic or drug-induced coma;
8. HF in combination with other therapies such as extracorporeal membrane oxygenation (ECMO) and the molecular adsorption recirculation system (MARS).^{12,13}

Practical guidelines for prescription²

Since the concentration of solutes in the filtrate is the same as in the plasma, biochemistry is controlled by removing large volumes of filtrate and replacing them with electrolyte-containing fluid (HF replacement fluid). As most solutes are distributed within the extracellular and intracellular fluid compartments (total body water), the exchange volume of filtration necessary to control biochemistry relates to total body water. Clinical experience has shown that a turnover of approximately 50% of body weight in 24 h is usually adequate for CVVH.

The extracorporeal circuit requires good central venous access, usually via a dual-lumen catheter, to allow the high blood flows necessary to prevent clotting in the haemofilter. Suggested catheter sizes in French gauge (FG) are shown in Table 2.

For neonates a 5-FG dual-lumen catheter may be adequate, and access can be obtained via the umbilical vein.¹⁴ A single-lumen catheter using a 'single needle' for CVVHD in very low birth weight infants has also been described,¹⁵ but this method may be compromised by high recirculation rates with most available systems. However, the smaller the access, the greater the problems.¹⁶ It is possible to consider placing two small single-lumen catheters in different central veins.

A low blood flow rate, high haematocrit and high plasma protein concentration will limit the rate at which filtration can occur and solutes (particularly of higher molecular weight) are removed. For a given blood flow rate, pre-dilution results in higher clearance of solutes than does post-dilution,¹⁷ but at the expense of greater use of replacement fluid (approximately 20–50% more). Pre-dilution has the potential for extending filter life.

As with HD, the blood volume in the extracorporeal circuit should be less than 10% of the patient's circulatory volume. Blood flow of 6–9 ml/kg/min or 8% of circulating blood volume prevents excessive haemoconcentration in the filter. Automated machines with appropriate accuracy for children are recommended for delivering the CRRT prescription safely,¹⁸ and have replaced pump-assisted haemofiltration using volumetric pumps.¹⁹

To achieve a 50% exchange of total body water in 24 h, an appropriate filter should be selected with a surface area of no more than the surface area of the patient (Table 3). Under post-dilution conditions, the filtration rate should never exceed one-third of the blood flow.

Several filter materials are now available. Cellulose acetate membranes have been replaced by synthetic membranes as they are regarded as more biocompatible, lowering the complement reaction and anticoagulation needs. The synthetic polysulphone membranes are also thought to aid convective clearance of solutes through solute drag.²⁰

A variety of replacement fluids are available, such as lactate, bicarbonate and buffer-free solutions. Bicarbonate or buffer-free solutions should be used in young infants and those intolerant of lactate. If a commercially available bicarbonate solution were freely available, then this would be the solution of choice. Careful monitoring of electrolytes, glucose and phosphate is essential, as the constituents vary between the solutions.

Anticoagulation

The goals of anticoagulation are to prevent clotting of the circuit and to maintain adequate clearances with minimal risk to the patient. Heparin is the standard anticoagulant in Europe, but the choice of dosage will depend upon the patient's coagulation status, adequacy of blood flow and blood viscosity. In most patients, heparin should be administered as an initial bolus (maximum 50 units/kg) at the time of connection to the extracorporeal circuit, followed by a continuous infusion of 0–30 units/kg/h. The activated clotting time (ACT) or whole blood activated partial thromboplastin time (aPPT) are usually used to monitor treatment. The optimal ACT during haemofiltration is 120–180 s but ACT is system and clotting bottle specific, so careful checking of manufacturers' instructions on the unheparinized range is essential. The aPPT should be between 1.2 and 1.5 times the respective baseline value. Some patients can be treated without heparin in the circuit.³

In those patients who are severely thrombocytopenic or where there is suspected heparin-induced thrombocytopenia, alternative treatment with a recombinant hirudin may be considered.^{21,22} These compounds exhibit their anticoagulant effect by inactivating fibrin-bound thrombin, but adjustments are required in renal impairment.

Regional anticoagulation with citrate has been favoured by some centres.^{23,24} Sodium citrate chelates the ionized calcium necessary for the coagulation cascade and systemic anticoagulation is avoided by infusing calcium through a separate central line. The disadvantages include the possibility of various acid-base and electrolyte disturbances, including hypernatraemia, hypocalcaemia and metabolic alkalosis.

Suggested FG catheter sizes

Patient weight (kg)	Vascular access
2.5–10	6.5-FG dual-lumen (10 cm)
10–20	8-FG dual-lumen (15 cm)
> 20	10.8-FG or larger dual lumen (20 cm)

Table 2

Suggested maximum filtration rates

Patient weight (kg)	Maximum filtration rate (ml/h)
< 8.5	250
8.5–20	500
> 20	2000

Table 3

Adjustment of the prescription

Any formula for the prescription of HF is at best an approximation or starting point, as the needs will be determined by many unmeasured variables, such as the rate of solute production, nutritional intake and the actual volumes of the extracellular fluid and intracellular fluid compartments. Each unit should have a standard protocol for initiation of the therapy but adjustments to the prescription will need to be based upon clinical, biochemical and technical factors.

If only fluid removal is required, then relatively low rates of filtration are needed, often referred to as slow continuous ultrafiltration (SCUF). There will be negligible solute removal under these circumstances.

Correction of 'uraemia' and electrolyte disturbance requires the turnover of large volumes per kilogram body weight, typically of the order of 50% of body weight per day for post-dilution and 75% for pre-dilution (approximately 20–30 ml/kg/h).

In catabolic patients, the clearances achieved with standard CVVH may not be sufficient. Solute removal may be increased by attempting 'high-volume exchange', but this may be limited by the practical problems of paediatric patients with limitations of vascular access and haemoconcentration in the filter. In these cases, small solute clearances can be maximized by establishing diffusive mass transport via a dialysis circuit. This can be performed with CVVHDF or without an additional major ultrafiltration component (CVVHD). The latter technique requires an additional pump to achieve separate control of the dialysate in- and out-flow, and of the replacement fluid flow. The new machines include this as an automated feature, making switching between CVVH/CVVHD and CVVHDF easy and safe. CVVH substitution fluid bags can be used as dialysis fluid. Dialysis fluid flow should be 2–3 times the blood flow if maximal efficacy is desired. This setting requires frequent manual bag exchanges and continuous supervision of the system. For practical purposes, the HD component can be added for several hours per day to a CVVH regimen.

CVVHD has recently been recommended as the method of choice for the treatment of inborn errors of metabolism, since it supplies maximal clearance of ammonium and other neurotoxic metabolites. When CVVHD is unavailable, large volume turnover (exchange) of body water with CVVH will provide the next best therapy. Rates of up to 100 ml/kg/h have been reported.²⁵ If possible, the blood pump speed also needs to be increased.

When high turnover and blood flow rates are in use, patients should be carefully monitored for hypothermia, hypokalaemia and circulatory failure. Hypothermia may need to be treated with an external warming blanket and hypokalaemia will require replacement. Blood flow should not be increased if the patient develops cardiovascular instability.

Complications

HF is most commonly used in sick septic children, many of whom will be on pressor therapy. Care should have been taken to prevent further risk of *hypotension* by minimizing the amount of blood in the extracorporeal circuit. Blood priming of the HF circuit may be necessary at the outset and especially in patients who weigh 10 kg or below. Fluid removal is obviously adjusted according to the patient's clinical state during the treatment. It is uncertain what effect HF circuits have on the concentrations

of pressor agents in the blood and hence their effectiveness. A drop in blood pressure has been observed in inotropic dependent patients, who often require their increase at the outset of treatment. However, this is often transitory.

Clotting of the filter and lines is one of the commonest complications and, again, is related to the patient's changing clinical status and problems with anticoagulation. This complication occurred in 24% of 89 patients treated with CVVH in a 2-year local audit (B. Harvey, unpublished observations).

Other potential complications of *bleeding*, *anticoagulation toxicity* and *infection* appear to be minimal. Air embolism is a rare but preventable complication of extracorporeal circuits, and is greatly reduced with the proper use of automated machinery.

A more significant drawback to the use of HF is the *technical complexity* and *high cost* of this therapy. Some centres may not be able to afford to establish an HF programme for this reason. In addition to the expensive equipment, the rate limiting function may be nurses trained and confident to use the HF circuit, especially in general PICUs where the need for CVVH is intermittent.¹² This may require innovative ways of support, such as a renal critical care educator.⁸

Nutrition

While HF allows for optimization of nutritional support in patients with high catabolic states (e.g. sepsis and ARF), it also contributes to the development of a negative nitrogen balance through the loss of free amino acids and peptides across haemofilters.^{3,26,27} The standard administration of 1.5 g/kg/day of protein is inadequate in most paediatric patients undergoing HF. Each patient's nutrition should be tailored to meet their overall needs with the aim of promoting an anabolic state, and the assistance of an experienced dietician is essential. It is clear that improved nutrition is associated with decreased morbidity in adult patients.²⁸

Currently, we suggest 2.5–3 g/kg/day of protein, with daily calorie intake 20–30% above normal resting energy expenditure in the form of total parenteral nutrition or better enteral feeds.²⁹

Special applications of haemofiltration

CVVH with ECMO

The best results appear to be achieved when pre-diluted fully automated CVVH is used, attached to the venous (outflow from patient) side of the ECMO circuit.¹² This appears to reduce problems of shunting blood around the oxygenator and overcomes the problems of the increased haematocrit that may be associated with ECMO. It also reduces the complications of excessive fluid and solute clearances, with a free flow when systemic haemofilters are used in line with the ECMO circuit. When using CVVH in the suggested configuration, the 'pigtailed' provide access with very little resistance, causing the arterial and venous pressure alarms to activate and shut down the circuit. Therefore, three-way taps are used to create more resistance to flow into and out of the CVVH circuit. When treating neonatal patients, the ECMO circuit increases the extracorporeal blood volume very significantly. Therefore, the blood pump speed should be calculated, taking into account the patient's blood volume and the priming volume of the ECMO circuit.

Inborn errors of metabolism²⁹

CRRT is an efficient adjuvant therapy for the acute treatment of inborn errors of metabolism. Both ammonia, which is elevated in urea cycle defects and some organic acidurias, and branched chain amino acids, which are elevated in maple syrup urine disease, are effectively cleared. As the first few hours of CRRT typically remove ammonia from the blood at a rate that is only 5–15% of that achieved with HD, the initial dialytic treatment of severe hyperammonaemia (e.g. blood ammonia levels more than 1000 µg/dl) should be HD with transition to CRRT once the serum ammonia is under 200 µg/dl. The combined use of HD and CRRT results in improved control of hyperammonaemia and prevents the rebound of serum ammonia levels seen with intermittent therapy. In patients with less severe hyperammonaemia, CRRT alone can be used as initial therapy.

As the goal of CRRT in patients with metabolic diseases is the rapid removal of toxic metabolites such as ammonia, the CRRT prescription should be altered to maximize clearance of these molecules. The blood flow rate should be increased to 7–10 ml/kg/min where possible, and the dialysate flow rate increased to 3000 ml/h/1.73 m². With these increased flow rates, care must be taken that patients do not develop hypophosphataemia, and a phosphate-containing dialysate is recommended for all patients with inborn errors of metabolism receiving CRRT.

Infants receiving CRRT for inborn errors of metabolism are at increased risk of developing hypothermia due to their small size and the higher blood flow rates needed for adequate clearance of toxic metabolites. Preventative measures such as heat lamps, warming blankets, warming of the circuit tubing and/or the use of an in-line blood warmer should be employed with the initiation of CRRT. In addition to HD and/or CRRT, appropriate pharmacological therapy should be initiated as soon as possible, so that the primary disease can be controlled.

It should be noted that CRRT has been shown effectively to clear components important in alternative pathways of ammonia excretion, such as glutamine and glycine. It is also likely, given the molecular size of the pharmacological agents used to treat metabolic disorders, that there is substantial clearance of these agents during therapy; thus, the administration of increased doses of these agents should be considered. Unlike nutritional supplementation that is required in ARF, the treatment of inborn errors of metabolism often requires significant protein restriction. Many of these children have otherwise normal renal function, which necessitates careful attention to the composition of filter replacement fluid to avoid electrolyte depletion.

Outcome

The impact of HF on outcomes of children treated in the PICU is highly controversial due to the paucity of randomized controlled trials. Smoyer et al identified the use of pressor drugs as being correlated with poor survival during paediatric HF.^{30,31} This observation was also supported by Bunchman et al and others.^{3,32} However, pressor drugs such as dopamine and adrenaline (epinephrine) are widely used in these very sick patients (85% in our own local series¹²) and hence appear to have little role in determining outcome. Recent retrospective paediatric series have found a relationship between mortality and the higher fluid overload when starting HF.^{10,33,34} Mortality and morbidity will

be influenced by the patient population being treated¹² and only multicentre trials or registries using agreed scoring systems will provide the answers to the questions to exactly when, how much and for how long HF therapy should be applied. ♦

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Practice points

- HF can be an efficient, reliable and safe form of RRT in the PICU, especially for haemodynamically unstable children
- The use of HF has expanded beyond the scope of ARF, but close cooperation is required between intensive care and nephrology teams so that optimal therapy can be delivered and solute clearance and fluid removal targets achieved
- HF is a costly technique which requires good vascular access and nursing staff familiar with the technique
- HF may lower blood levels of essential ions and requires careful monitoring, but its effects on drug levels such as pressor agents and antibiotics is largely unknown

Intracranial pressure monitoring in comatose children

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Abstract

Coma may be associated with raised intracranial pressure (ICP), with a causative relationship in some cases. ICP monitoring provides an objective measurement of intracranial pressure and allows the ICP response to specific interventions to be directly observed. A combination of ICP and invasive arterial pressure monitoring provides a measure of the cerebral perfusion pressure (CPP), which is an important parameter in determining cerebral blood flow. Despite widespread use of ICP monitoring in certain causes of coma, most notably traumatic brain injury, the use of ICP monitoring is not proven to improve outcome in any cause of coma. This review explores the current medical literature regarding the uses of ICP monitoring in the paediatric population.

Keywords brain injuries; cerebrospinal fluid shunts; child; coma; intensive care units; intracranial hypertension; meningitis; paediatric

Introduction

An acutely ill child with a reduced level of consciousness can present a significant management challenge to the clinician in charge of their care. Unconsciousness or coma can result from a wide variety of clinical disease processes, both traumatic and non-traumatic, and each has their unique requirements in terms of treatment and management (Table 1). These children are often managed on paediatric intensive care units (PICUs) and require invasive ventilation for airway protection, as well as ongoing ventilatory support for the underlying disease process. Clinical assessment of their conscious level then becomes more difficult with the introduction of sedative drugs and, where necessary, neuromuscular blockade. The clinical concern at this point is whether intracranial hypertension is present and, if so, if treatment of this is warranted.

Intracranial pressure (ICP) can be measured by the insertion of an intraventricular or an intraparenchymal pressure monitoring device in the brain. This can tell the clinician both the ICP and also, when combined with invasive arterial monitoring, the calculated cerebral perfusion pressure [CPP = mean arterial

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Causes of coma with raised intracranial pressure in children

Traumatic

- **Acute traumatic head injury**
 - Subdural haematoma
 - Extradural haematoma
 - Intracerebral bleed
 - Diffuse axonal injury

Non-traumatic

- **Primary intracranial disease**
 - Acute hydrocephalus: obstructive, communicating
 - Infections: meningitis, encephalitis, cerebral malaria
 - Seizures
 - Tumours
 - Inflammatory: acute disseminated encephalomyelitis (ADEM)
 - Vascular disorders: arteriovenous malformations, aneurysms, bleeding diathesis
- **Systemic disease with coma**
 - Acute encephalopathy: metabolic disorders, diabetic ketoacidosis, hyperammonaemia, hepatic encephalopathy
 - Renal disease: haemolytic uraemic syndrome
 - Hypertensive encephalopathy
 - Hypoxic-ischaemic encephalopathies: drowning, asphyxia, post cardiac arrest
 - Toxic exposure: lead, vitamin A overdose, atraxotoxin (spider bite)

Table 1

pressure (MAP) – ICP]. In conditions associated with a loss of cerebral autoregulation, such as severe bacterial meningitis, there will be a linear relationship between CPP and cerebral blood flow. Preservation of an adequate CPP is central to neuroprotection. The focus of this review is the question of whether ICP *should* be measured and whether there is evidence that measurement of ICP improves outcome for the patient.

We will review the pathophysiology of intracranial hypertension, explore the methods of clinically assessing its presence and appraise the literature with regards to the role of ICP monitoring in specific conditions.

Pathophysiology of intracranial hypertension

The cranial vault is a rigid structure containing blood, CSF and brain parenchyma. The Monroe-Kellie concept describes the relationship of these three substances to each other. If one of the components increases, then there must be a corresponding reduction in the other two. In the normal healthy brain, autoregulation processes can compensate for the increase in volume of one substance by restricting the other two. However the compliance of the brain, defined as the ability to withstand changes in volume without changes in pressure, is only stable up to a certain volume. Thereafter an additional small increase in volume can lead to a significantly greater increase in pressure (Figure 1).¹ This excess pressure is defined as intracranial hypertension.

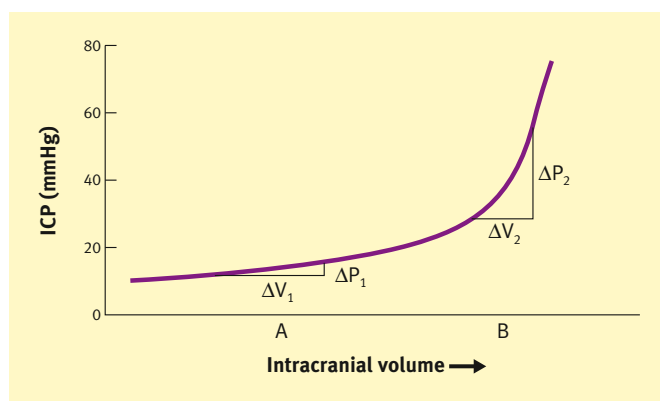


Figure 1 Relationship of intracranial volume to intracranial pressure (ICP). At normal brain compliance ICP increases only slightly as intracranial volume increases (area A). A further increase in volume results in a steep rise in ICP (area B).

Examples of disease processes affecting the intracranial components include: traumatic brain injury leading to extradural haematomas (blood); cytotoxic oedema in acute hepatic encephalopathy (brain parenchyma); and communicating hydrocephalus [cerebrospinal fluid (CSF)] (Table 2).

Principles of management of raised intracranial hypertension

A reduction of pressure inside the skull can be achieved by using a number of general measures and more specific therapies directed at the different disease processes (Table 2).

Pathophysiology of raised intracranial pressure and management options

Component	Cause of raised ICP	Management
Blood	<i>Local</i>	
	Subdural haematoma	Surgery
	Extradural haematoma	Surgery
	Subarachnoid haemorrhage	External ventricular drain
	Intracerebral bleed	Surgery
	<i>General</i>	
	Hyperaemia	Titrated hyperventilation
CSF	Hydrocephalus	External ventricular drain, lumbar puncture
Brain	Diffuse axonal injury	Osmotherapy
	Cerebral oedema	Osmotherapy
Any		Decompressive craniectomy
Other	Seizures	Phenytoin, barbiturate
	Fever	Cool to normothermia

Table 2

If a localized collection of blood is the predominant cause, then urgent neurosurgical evacuation is the treatment of choice. Swelling caused by oedema of the brain parenchyma can respond to osmotic therapy (3% saline or mannitol). Excess CSF, as in hydrocephalus, can be treated by removal of CSF via a drain (intraventricular or lumbar) or a more permanent shunt (ventriculo-peritoneal shunt). General measures found to decrease ICP include the use of sedation, the prevention of hypoxia and hypercarbia, and the avoidance of hyperthermia. Although hypothermia therapy is known to decrease ICP in traumatic brain injury, its routine early use in children with severe traumatic brain injury does not improve outcome and may even be detrimental.² Hypothermia has been shown to improve outcome in adults with hypoxic-ischaemic encephalopathy following cardiac arrest and in newborns with hypoxic-ischaemic encephalopathy, but it is unknown whether this is mediated through a change in ICP.

The use of surgical decompressive craniectomy in the treatment of acute, self-limiting brain swelling makes theoretical sense in allowing expansion of intracranial contents with a blunted response in ICP. Current clinical trials are ongoing to ascertain its use and timing in the treatment of intracranial hypertension associated with traumatic brain injury. It could have a role in conditions such as cerebral oedema complicating diabetic ketoacidosis, although it is unlikely that adequately powered trials will be undertaken given the rarity of the condition.

Blind use of the treatment interventions described in Table 2 to lower ICP without monitoring of ICP is not recommended.

Assessment of intracranial pressure

Clinical assessment

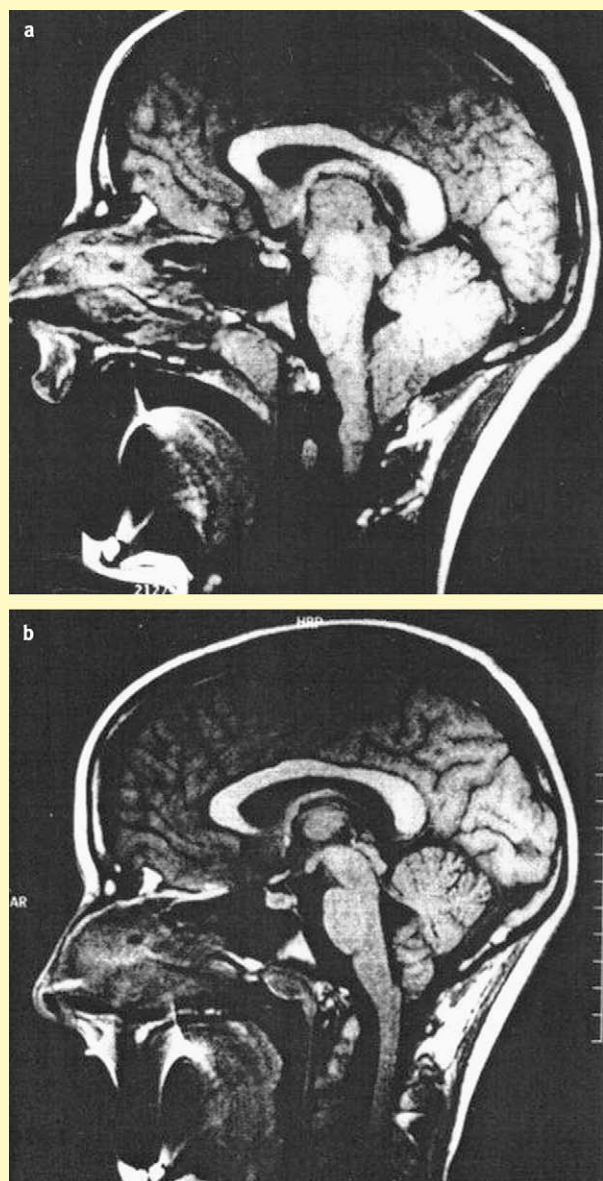
The presence of headache, diplopia, decreased conscious level, abnormal posturing, excessive cranial enlargement and papilloedema can all indicate raised ICP, but each lacks a high degree of sensitivity or specificity. Acute intracranial hypertension is often not associated with papilloedema. Signs of impending herniation of the brain result from compression of cranial nerves or the brain stem from increased cerebral swelling. This can cause an ipsilateral dilated pupil if the cerebral swelling is one sided or bilateral dilated pupils if generalized (IIIrd cranial nerve sign). The Cushing's response is a reduced respiratory rate, bradycardia and hypertension, and is caused by brain stem compression.¹

In infants, the open fontanelle can theoretically be palpated to assess underlying pressure in the cranial vault. Mechanical devices have been developed to try and measure the open fontanelle pressure but have not been accepted widely into clinical practice.

Brain imaging

Computerized tomography (CT) scanning allows quick identification of mass lesions and structural abnormalities in the brain, including the detection of hydrocephalus. It can guide neurosurgeons to the need for urgent surgical intervention. The presence of cerebral oedema may be suggested, however a 'normal' CT scan does not rule out significant intracranial hypertension.³

Magnetic resonance imaging (MRI) requires a longer scanning time than CT and is therefore often not performed in the initial acute phase of admission until a child is stable. It does, however, give excellent information regarding grey and white matter changes in the brain, and in cases of both traumatic and



a MRI demonstrating cerebellar tonsillar herniation in a patient with severe meningitis. **b** MRI of same patient *after lowering of ICP*, demonstrating reversal of cerebellar tonsillar herniation (Reproduced with permission of Wiley Interscience from Grände et al.⁴).

Figure 2

non-traumatic coma can help in the diagnosis and prognosis of intracranial pathology. It is also able to demonstrate tonsillar herniation in severe cases (Figure 2).⁴ However, similar to CT scan, it cannot on its own exclude intracranial hypertension.

ICP monitoring

Types and benefits

Intraventricular catheter [external ventricular drain (EVD)]

Currently available monitoring devices include an intraventricular drain connected to an external pressure transducer. The



Figure 3 Camino® intraparenchymal pressure transducer in a ventilated child after a severe head injury.

advantages of this device are that in addition to the continuous monitoring of ICP, there is the ability to drain CSF as a therapy to reduce ICP. However, placement of an intraventricular drain can be technically difficult if the ventricles are narrow and compressed. It is possible to re-zero an intraventricular drain externally if the accuracy starts to drift.^{3,5}

Intraparenchymal device

Intraparenchymal transducers can be classified as solid-state, based on pressure-sensitive resistors, or fibre optic, and are placed via a burr hole into the brain parenchyma. Unfortunately, these catheters cannot be recalibrated once inserted into the brain, although the low risk of drift with current fibre optic pressure transducer in the first 5 days has enabled them to be used with more confidence than older devices (Figure 3).

Both intraventricular and intraparenchymal ICP allow continuous, realtime assessment of changes in ICP.

ICP can be monitored by the insertion of subarachnoid, subdural and epidural transducers, but these are all used less frequently than the intraventricular and intraparenchymal devices as they give less reliable readings.

Risks

ICP monitoring has been shown to be both safe and accurate in repeated studies in the paediatric population.

The main concerns are the risks of infection, bleeding, device accuracy and drift of measurement over time. Infection rates have been consistently shown to be low (0.3–1.5%) in paediatric studies investigating both intraparenchymal and intraventricular devices, where devices were left in situ for a median of 3 days. A large adult study found that the infection risk increased after 5 days of insertion to a rate of 5–7%.⁵

The risk of bleeding has been reported to be up to four times higher with intraventricular drains than intraparenchymal devices (17.6% versus 6.5%). Another larger study reported an incidence of only 0.3% with mostly intraparenchymal devices. In this study of 303 paediatric patients, displacement of catheters occurred in 1% of cases and malfunction in only 2.6%.⁶

In patients at risk of bleeding, e.g. those with fulminant hepatic failure and severe coagulopathy, the risk:benefit ratio may result in ICP monitoring not being undertaken.

Role of ICP monitoring in specific conditions

Traumatic coma

Neurological injury can occur in two distinct periods. There is the initial primary injury, comprising axonal injury, brain contusion, laceration, haemorrhage and shearing injury.⁷ Prevention is related to avoiding injury and public health interventions, such as wearing helmets when cycling. Secondary injury may be exacerbated by hypoxia, hypotension, hyperthermia, seizure activity and intracranial hypertension. An 'ABC' approach to resuscitation will address the issues of hypoxia and hypotension, and stabilization of other injuries.⁷ Failure to treat the causes of secondary injury can lead to further ischaemia and neuronal damage. Intracranial hypertension can occur because of mass effect from a collection of blood (e.g. subdural or extradural haematoma). These are regarded as neurosurgical emergencies requiring urgent surgery to evacuate the blood. Further intracranial hypertension can occur over the subsequent hours and days due to cerebral oedema. This swelling can be difficult to detect clinically and, although CT and clinical examination are useful, they cannot be relied upon to give an accurate assessment of the ICP. It is at this point in severe traumatic brain injury [defined as a Glasgow coma score (GCS) less than 8] that ICP monitoring is advised in the current international guidelines for management of paediatric traumatic brain injury.⁸ However, a recent UK study identified that only 60% of eligible children had ICP monitoring, with large centre-to-centre variation.⁹

Intraventricular catheter measurement of ICP is recommended⁸ as it allows both monitoring of ICP and drainage of CSF to lower ICP, but is infrequently undertaken in the UK.⁹

There is no high level evidence supporting the use of ICP monitoring in traumatic brain injury or indeed other causes of paediatric coma.¹⁰ However, studies have repeatedly shown that persistently high ICP or low CPP are associated with poor neurological outcome or death.^{11–13} On the basis of this approach, Chambers et al¹³ have suggested age-related CPP targets (Table 3). Whether achieving these targets will improve outcome should be a focus of neurointensive care research.

One argument for measuring ICP is to have a marker of response when applying an intervention for intracranial

hypertension. Hyperosmolar therapy (3% sodium chloride or mannitol), craniectomy, thiopentone infusion and hyperventilation (for acute episodes only) are advocated to treat acute rises in ICP or signs of impending coning. If these treatments are given without knowing the changes made to ICP, then there is a risk of over or under treatment with consequential adverse events. Despite this, recent audit data suggest that as many as 17% of children with traumatic brain injury receive interventions targeting a raised ICP in the absence of ICP monitoring.⁹

There is good evidence from both the UK and the US that ICP monitoring is undertaken less often in infants.^{9,14} Reasons cited for not monitoring this group include potential difficulty in fixing a bolt through a thin skull vault, and the fact that an open fontanelle and suture lines allow a non-invasive estimation of ICP and also provide some 'decompression' by expansion of the skull vault, preventing a marked rise in ICP. However, the evidence for this is poor and studies have not shown that clinical assessment of the fontanelle is a reliable indicator of ICP. Serious consideration should be given to ICP monitoring in this group.

In conclusion, ICP monitoring in traumatic coma is a useful tool to identify a group of children with raised ICP who have a worse prognosis and can be targeted for interventions aimed at lowering ICP and improving CPP. It also allows the clinician to assess the response to treatment modalities in managing intracranial hypertension. Its use is encouraged and recommended internationally with particular emphasis on the benefit of an intraventricular catheter giving the option of CSF drainage.

Non-traumatic coma

Hypoxic–ischaemic encephalopathy

Acute hypoxic brain injury can result in severe neurological damage and death. This injury is most commonly seen in children after cardiorespiratory arrest. Causes of respiratory arrest in children include severe status asthmaticus, near drowning and asphyxiation from hanging. Cardiac arrest is usually secondary to a respiratory aetiology but cardiac arrhythmias and ischaemia are seen especially in children with congenital heart disease.

A number of studies were carried out using ICP monitoring in children after they had been resuscitated from near-drowning. Twenty years ago there was enthusiasm for its use, with some studies showing that early ICP levels were useful at predicting outcome.¹⁵ However, as further studies were performed, it became clear that neither the initial ICP measurement or management of rises in ICP and maintenance in CPP resulted in improved outcome.^{16,17} The potential for neurological survival of these children appears to be related to the severity of the primary insult rather than the subsequent intracranial hypertension which follows.^{17,18} Few studies have been published over the last 10 years in the use of ICP monitoring in this condition, but few centres currently advocate ICP monitoring for coma associated with hypoxic brain injury.

Within a group of patients with hypoxic–ischaemic encephalopathy it is conceivable that there is a subgroup of patients, e.g. those with less severe initial insults, who may benefit from ICP monitoring, but current evidence does not support this.

Age-related cerebral perfusion pressure for traumatic brain injury¹³

Age (years)	Cerebral perfusion pressure target (mmHg)
0–2	Unclear, likely >40
2–6	>53
7–10	>63
11–15	>66
>16	>70 (adult data)

Table 3

Acute hepatic encephalopathy

Intracranial hypertension can develop in patients with acute liver failure, particularly those with grade III/IV hepatic encephalopathy. Subsequent development of cerebral herniation and brain stem death is the most frequent cause of death in this patient population.

The precise aetiology is still not completely understood but it is considered to be related to cytotoxic cerebral oedema induced by hyperammonaemia and other toxic metabolites. Cerebral blood flow may be increased above physiological need and contribute to vasogenic oedema and raised ICP.

Curative treatment for acute liver failure is liver transplantation. Intensive care management of the preceding multiorgan failure and intracranial hypertension can potentially bridge the patient to the time an organ becomes available.

Controversy exists as to the use of ICP monitoring in this patient group due to the higher complication rate of intracranial haemorrhage. Recent adult data report an incidence of 10% which has halved from more historical studies.¹⁹ This is likely to be due to more aggressive use of fresh frozen plasma (FFP), cryoprecipitate, platelets and recombinant factor VIIa before insertion of the ICP monitoring device. This practice, however, involves large fluid volumes potentially increasing the risks of cerebral oedema. Extracorporeal fluid removal using continuous venovenous haemofiltration (CVVH) or plasma filtration can prevent fluid overload. Some centres have placed subdural catheters as a trade-off between reduced bleeding risk but with a less accurate ICP result compared with intraparenchymal devices. In a recent study, ICP monitoring was performed in 28% (92/332) of adults with acute liver failure but was more likely in those being listed for transplantation.¹⁹ Its use was associated with a significant increase in the use of mannitol, barbiturates and vasopressors. There were two deaths where the insertion of the ICP device may have directly contributed and there was also wide variation in its use between centres.

Reye syndrome is a specific cause of acute encephalopathy in children associated with acute hepatic failure. It is associated with a high mortality although its incidence has decreased significantly. The use of ICP monitoring in managing these children was advocated in the 1980s based on a number of observational studies. These suggested that peak and initial ICP measurements were not useful in predicting outcome but that survival with good neurological outcome could be achieved if CPP could be maintained by aggressive ICP reduction and maintenance of systemic blood pressure to a level more than 40 mmHg.²⁰

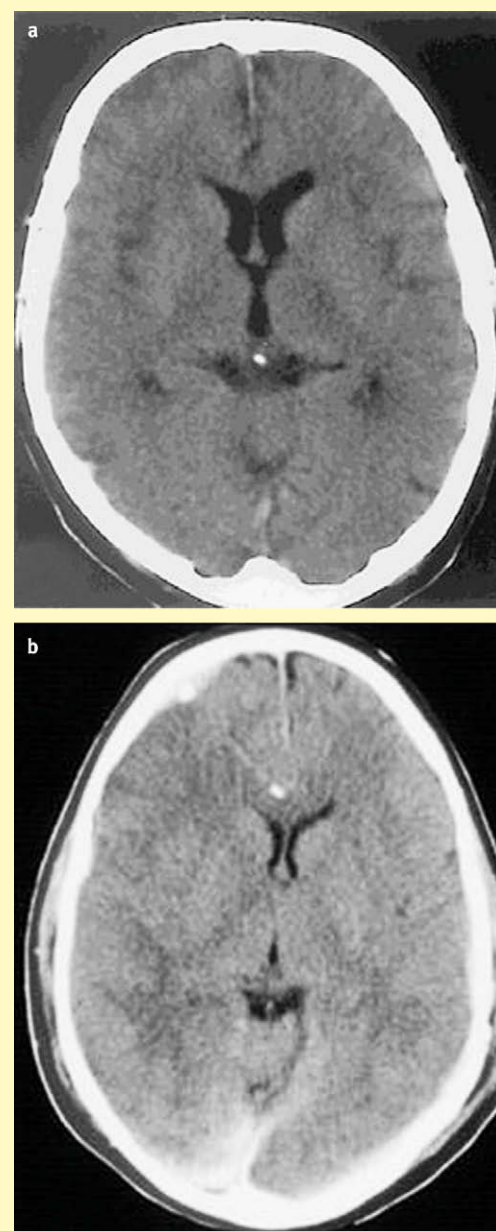
There are no randomized controlled trials in any age group and the real risk of intracranial bleeding and the continued reports of deaths in the adult population associated with ICP monitoring for acute liver failure may continue to limit its use in paediatric patients.

Other acute 'metabolic' encephalopathies associated with intracranial hypertension, such as hyperammonaemia associated with a urea cycle disorder, and diabetic ketoacidosis may be conditions which would benefit from ICP monitoring. There is currently little firm clinical data to support its use.

Bacterial meningitis

Children with bacterial meningitis commonly develop raised ICP and those who die often demonstrate evidence of raised ICP and

cerebral herniation at port-mortem examination. In severe bacterial meningitis there is a loss of cerebral autoregulation in that there is a loss of the normal adjustment in cerebral vascular tone that allows cerebral blood flow to be held constant across a physiological range of arterial blood pressure.²¹ Cerebral blood flow becomes pressure dependent and changes in either MAP or ICP can have a profound influence on cerebral blood flow. Equally, an increase in cerebral blood flow to supra-physiological levels as a consequence of a marked rise in arterial pressure will lead



a CT scan of patient with meningitis 70 min after clinical herniation and an ICP of 90 mmHg. Note the 'normal' sized lateral ventricles.

b Comparison CT of a patient after a traumatic head injury demonstrating cerebral oedema and narrowed lateral ventricles (Reproduced with permission of Springer from Winkler et al.³)

Figure 4

to an increase in ICP (as a consequence of an expansion of the intracranial vascular compartment).

A failure of CSF reabsorption may occur as a result of obstruction of the aqueduct of Sylvius by thick inflammatory exudates. Whereas a reduction in the size of the lateral ventricles on CT scan may provide a clue that ICP is raised in a patient with traumatic brain injury, this is not the case in bacterial meningitis. Herniation may occur as a result of severe intracranial hypertension despite the appearance of 'normal' sized lateral ventricles (Figure 4).

Drainage of CSF in this situation will have a potent effect in lowering ICP and should be considered in any child with clinically suspected intracranial hypertension secondary to bacterial meningitis. There are no randomized controlled trials of ICP monitoring or ICP targeted intervention in patients with bacterial meningitis, but a number of reports suggest that ICP monitoring is being used more often in this setting, albeit in a limited number of centres.²² A preliminary report from France reports success with CSF drainage.²³

There are two large studies in the US examining the use of ICP monitoring and effect on survival in children with bacterial meningitis.^{22,24} Although 80% of PICU admissions for meningitis were under 1 year of age, the majority of ICP monitoring was undertaken in the 5–15-year-old group. ICP monitoring was rare in both studies (7% and 14%), although there was considerable centre-to-centre variability in use of ICP monitoring. Survival was no different in centres using more aggressive ICP monitoring. UK data from the PICANet database (national data from PICU admissions in UK hospitals) for 2003–2004 suggest that only 5.9% of children admitted to PICU with a diagnosis of bacterial meningitis underwent ICP monitoring (14/238) (R. Parslow, personal communication).

Conclusion

Coma in children can occur as a result of a wide variety of conditions, with many associated with life-threatening intracranial hypertension. Recognition and monitoring of intracranial hypertension is unreliable using clinical examination or brain imaging. The use of invasive ICP monitoring can be helpful in recognizing the development of intracranial hypertension and in guiding therapeutic interventions. However, the evidence base for monitoring of ICP in children with coma of any aetiology is very limited with no randomized controlled trials. Despite a lack of high level evidence, its use in severe traumatic brain injury is widely accepted and recommended through international guidelines. In non-traumatic coma there is no consensus for its use. There is early emerging evidence suggesting that it may have a role in bacterial meningitis. Intracranial hypertension in acute hepatic encephalopathy is associated with death in a number of patients who are awaiting a liver transplant. Concerns surrounding the risk of intracranial bleeding have prevented widespread use of ICP monitoring, although some centres undertake it routinely and describe good results.

Decompressive craniectomy may become more widely used as an intervention to limit intracranial hypertension in those patients who have an acute reversible process associated with a life-threatening elevation in ICP, e.g. the child with cerebral oedema associated with diabetic ketoacidosis. ◆

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Practice points

- CT scan does not provide a reliable measure of ICP
- In children with severe traumatic brain injury (GCS < 8) ICP monitoring should be undertaken
- ICP monitoring allows the response of specific interventions to be directly observed
- The gold-standard for measuring ICP is the ventricular catheter
- Drainage of CSF via a ventricular catheter is effective at lowering ICP

ADHD and the paediatrician: a practical guide

Paul Davis

Azra Sabir

Abstract

Attention Deficit Hyperactivity Disorder (DSM-IV) and Hyperkinetic Disorder (ICD-10) are common conditions with a high morbidity which impact on the lives of the affected children, their families and schools, and have important implications for wider society. Behavioural, psychological and medical treatments are available and there is a sound evidence base for drug treatments. NICE guidance is available. This review summarises what is known about the condition, available treatments and common dilemmas which may be faced by a general or community paediatrician who has some interest in behavioural disorders.

Keywords ADHD; Behavioural disorders; DAMP; Hyperkinetic disorder; stimulants

Definition

Attention deficit hyperactivity disorder (ADHD) is a pervasive disorder of attention control, usually with hyperactivity and impulsivity. It is present from an early age, causes significant impairment in performance and is present in at least two settings (usually home and school). The clinical features are not adequately explained by some other process, e.g. a neurological illness, maltreatment, learning disability or pervasive developmental disorder. The coexistence of other disorders does not preclude the diagnosis of ADHD but there should be caution in proceeding with diagnosis, mindful of the fact that other conditions can effectively mimic the ADHD phenotype but may need different management strategies.

ADHD is most commonly of the combined type (both inattention and hyperactivity present) and less commonly of the predominantly inattentive type ('ADD minus H') or the predominantly hyperactive-impulsive type; the latter two are quite likely to be underdiagnosed.

It is a common disorder with a population prevalence (using DSM-IV criteria) of approximately 3–5% of children, of whom about one-fifth will be severely impaired (1% of school-age children). Children are believed to have a genetic predisposition to ADHD, although the clinical manifestation of the problem is in

part dependent on environmental factors such as parental management styles, social stresses or educational resources.

Aetiology

The specific aetiology is unknown but various studies implicate dopaminergic and noradrenergic pathways in the brain, which is compatible with our current understanding of the mode of action of the common pharmaceutical agents that are effective in treating ADHD. There are undoubtedly genetic and environmental factors in the evolution of the condition and the extent to which it causes impairment, and these will vary from family to family. It is possible to demonstrate structural and functional changes in the brains of individuals with ADHD in the context of research but there is no reliable test for the condition and the diagnosis rests on clinical features.

Service models

Whilst the prevalence of ADHD has probably not changed greatly in recent years, the administrative prevalence has, probably due to greater recognition on the part of parents, teachers and doctors. The increasing number of requests for ADHD assessment has created service pressures around the UK and each area will have evolved a strategy (with greater or lesser degrees of planning) to address the problem. In some areas, specialist child and adolescent mental health services (CAMHS) provide a service almost exclusively; in others paediatricians may have developed expertise in this field, working alone or in conjunction with their local CAMHS. The authors have adopted a joint clinic approach, attempting to harness the specialist skills and common interests of each professional group to provide a tailored service to patients.

There is considerable overlap in the skills of child and adolescent psychiatrists and paediatricians who have an interest in behavioural disorders. Both should possess the basic skills required to assess and diagnose ADHD, but as many patients deviate from the 'norm' and have various associated morbidities, the specialist skills in mental health or physical and developmental disorders will be needed in many cases and a joint clinic approach facilitates this.

Specialist CAMHS also usually involve a wider team with more extensive resources aimed at supporting children and their families in difficult situations and this may also be invaluable. The community child health team will also include a school health service, which will be instrumental in advocating for the child and meeting their health needs in school. Therefore, it is important that both professions work closely to provide a comprehensive service.

General practitioners (GPs) are seldom involved actively in the management of ADHD but they need to know when and how to refer appropriately, and it is reasonable to ask the GP to prescribe for children who are under regular review in secondary care. Some areas have 'shared care protocols' covering the prescription of ADHD medication.

Diagnostic criteria

DSM-IV and ICD-10 criteria are available (Tables 1 and 2).^{1,2} They are very similar but the more stringent requirement for the presence of all three core symptoms (inattention, hyperactivity and

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DSM-IV criteria for attention deficit hyperactivity disorder¹

I. Either A or B:

- A. Six or more of the following symptoms of inattention have been present for at least 6 months to a point that is disruptive and inappropriate for developmental level:
1. Often does not give close attention to details or makes careless mistakes in schoolwork, work or other activities
 2. Often has trouble keeping attention on tasks or play activities
 3. Often does not seem to listen when spoken to directly
 4. Often does not follow instructions and fails to finish schoolwork, chores or duties in the workplace (not due to oppositional behaviour or failure to understand instructions)
 5. Often has trouble organizing activities
 6. Often avoids, dislikes or doesn't want to do things that take a lot of mental effort for a long period of time (such as schoolwork or homework)
 7. Often loses things needed for tasks and activities (e.g. toys, school assignments, pencils, books, or tools)
 8. Is often easily distracted
 9. Is often forgetful in daily activities
- B. Six or more of the following symptoms of hyperactivity-impulsivity have been present for at least 6 months to an extent that is disruptive and inappropriate for developmental level:

Hyperactivity

1. Often fidgets with hands or feet or squirms in seat
2. Often gets up from seat when remaining in seat is expected
3. Often runs about or climbs when and where it is not appropriate (adolescents or adults may feel very restless)
4. Often has trouble playing or enjoying leisure activities quietly
5. Is often 'on the go' or often acts as if 'driven by a motor'
6. Often talks excessively

Impulsivity

1. Often blurts out answers before questions have been finished
2. Often has trouble waiting one's turn
3. Often interrupts or intrudes on others, e.g. butts into conversations or games

II. Some symptoms that cause impairment were present before age 7 years

III. Some impairment from the symptoms is present in two or more settings, e.g. at school/work and at home

IV. There must be clear evidence of significant impairment in social, school or work functioning.

V. The symptoms do not happen only during the course of a pervasive developmental disorder, schizophrenia or other psychotic disorder. The symptoms are not better accounted for by another mental disorder, e.g. mood disorder, anxiety disorder, dissociative disorder or a personality disorder

Based on these criteria, three types of ADHD are identified:

1. ADHD, *combined type*: if both criteria 1A and 1B are met for the past 6 months
2. ADHD, *predominantly inattentive type*: if criterion 1A is met but criterion 1B is not met for the past 6 months
3. ADHD, *predominantly hyperactive-impulsive type*: if criterion 1B is met but criterion 1A is not met for the past 6 months

Table 1

impulsivity), pervasiveness and exclusion criteria within the ICD-10 criteria means that ICD-10 defines a more morbid subgroup, whereas DSM-IV includes a far larger proportion of the population.

It may be helpful in a clinic setting to arrange the criteria as a 'checklist' but it is important to allow the child's carers (and the older child themselves) to describe their concerns in their own words without inhibition. The clinician should enquire about the child's functioning and degree of impairment in more detail as the criteria are explored, as opposed to slavishly 'ticking boxes'.

Diagnosis

ADHD is a clinical diagnosis and the cornerstone of diagnosis is the clinical history. The carers should be allowed to explain their

concerns fully. DSM-IV or ICD-10 criteria (Tables 1 and 2) should be explored and a detailed review should include past obstetric and medical history, family, social, developmental and educational histories, and a full systematic enquiry. Particular attention should be given to eliciting history of developmental delay, neurological abnormality (including seizures or tics), evidence of dyspraxia, pervasive developmental disorder or adverse social factors. Hearing loss should be asked about. There may be a family history of ADHD or autism. Due to the very rare association between stimulants and arrhythmias or sudden death, enquiry should be made about any relevant family history and, if necessary, an ECG obtained.

Corroboration of the impairment should be sought from several sources. Feedback about the child's school performance

ICD-10 criteria: attention deficit/hyperactivity disorder²

F90 Hyperkinetic disorders

G1 Inattention

At least six of the following symptoms of attention have persisted for at least 6 months, to a degree that is maladaptive and inconsistent with the developmental level of the child:

1. Often fails to give close attention to details, or makes careless errors in school work, work or other activities
2. Often fails to sustain attention in tasks or play activities
3. Often appears not to listen to what is being said to him or her
4. Often fails to follow through on instructions or to finish school work, chores, or duties in the workplace (not because of oppositional behaviour or failure to understand instructions)
5. Often impaired in organizing tasks and activities
6. Often avoids or strongly dislikes tasks, such as homework, that require sustained mental effort
7. Often loses things necessary for certain tasks and activities, such as school assignments, pencils, books, toys or tools
8. Often easily distracted by external stimuli
9. Often forgetful in the course of daily activities

G2 Hyperactivity

At least three of the following symptoms of hyperactivity have persisted for at least 6 months, to a degree that is maladaptive and inconsistent with the developmental level of the child:

1. Often fidgets with hands or feet or squirms on seat
2. Leaves seat in classroom or in other situations in which remaining seated is expected
3. Often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, only feelings of restlessness may be present)
4. Often unduly noisy in playing or has difficulty in engaging quietly in leisure activities
5. Exhibits a persistent pattern of excessive motor activity that is not substantially modified by social context or demands

G3 Impulsivity

At least one of the following symptoms of impulsivity has persisted for at least six months, to a degree that is maladaptive and inconsistent with the developmental level of the child:

1. Often blurts out answers before questions have been completed
2. Often fails to wait in lines or await turns in games or group situations
3. Often interrupts or intrudes on others, e.g. butts into others' conversations or games
4. Often talks excessively without appropriate response to social constraints

G4 Age of onset

Onset of the disorder is no later than the age of 7 years

G5 Pervasiveness

The criteria should be met for more than a single situation, e.g. the combination of inattention and hyperactivity should be present both at home and at school, or at both school and another setting where children are observed, such as a clinic. (Evidence for cross-situationality will ordinarily require information from more than one source; parental reports about classroom behaviour, for instance, are unlikely to be sufficient)

G6 Impact

The symptoms in G1 and G3 cause clinically significant distress or impairment in social, academic, or occupational functioning.

G7 Exclusion criteria

The disorder does not meet the criteria for pervasive developmental disorders (F84.-), manic episode (F30.-), depressive episode (F32.-) or anxiety disorders (F41.-)

Table 2

in particular is essential. If there are no significant concerns at school, there should be considerable doubt about whether the child has ADHD. In seeking information from schools it is important to emphasize the difference between oppositional behaviour ('naughtiness') and impairment in attention control. Whilst they can coexist, they are not the same thing, and 'well-behaved' children may still have great difficulty with attention control and be

underperforming as a result. This is particularly true in 'ADD minus H' cases. Grandparents, family members or close family friends may also have useful history to give.

Rating scales and scoring sheets are invaluable both in establishing the diagnosis and, particularly, for monitoring the child's response to interventions. Conners' questionnaires are simple to use and provide information on a range of difficulties, including

conduct and educational difficulties as well as ADHD. Various other rating scales are available which all have their attributes. It is best to become familiar with a few reliable 'tools' to assist diagnosis. All rating scales are to some extent subjective, so the responses need to be explored in more detail by thorough review of the history, and they should be obtained from as many sources as possible.

Clinic observation is essential, although there are pitfalls. Some children are 'on their best behaviour' in clinic and may not demonstrate the problems which are causing difficulty at home or in school. However, if a consultation is longer than about 20 min, the child's attention control difficulties will usually become apparent. Again, it is important to recognize that some children with ADD are neither hyperactive nor naughty.

As an aside, for children who already have a diagnosis, it is important to enquire whether they have had their medicine, as some parents have been known to withhold medication on clinic days so that the doctor will see them at their worst! This may particularly be an issue if the carers are seeking support for the Disability Living Allowance.

Whilst in clinic, a physical examination is indicated to screen for common physical conditions or co-morbidities, such as dyspraxia, anaemia, thyroid disorders and neurocutaneous syndromes. Baseline height, weight and blood pressure should be documented.

'In situ' observation in school is very helpful. The teachers may provide this information or a school visit may be carried out. If there is a well developed school health service then the school doctor or nurse may help with this.

Important co-morbidities

The following are common coexisting conditions in children with ADHD and should be considered in the initial and subsequent clinical assessments. Their presence may aggravate the impairment caused by ADHD and vice versa. Some may mimic aspects of ADHD and diagnosis may be difficult. If in doubt, extended assessment or a tertiary opinion is indicated. These conditions are not absolute contraindications to drug treatment of ADHD but response to treatment should be monitored closely as experience suggests that the response to medication is less predictable in some of these children.

- *Autistic spectrum disorder (ASD)/Asperger*. Said to be present in up to one-third of ADHD patients, although still underdiagnosed.
- *Dyspraxia/disorder of attention, motility control and perception (DAMP)*. If present, should lead to an occupational therapy or physiotherapy referral.
- *Dyslexia*. Usually addressed by schools.
- *Developmental delay/learning difficulty (LD)*. In younger children, a Griffiths developmental assessment may be helpful. Older children should be referred through education for formal educational psychology assessment. Baseline medical assessment should be as for developmental delay.
- *Tourette/tic disorders*. May need specialist mental health assessment.
- *Oppositional defiant disorder (ODD)/conduct disorder*. Common and likely to need to access services through CAMHS. Treating ADHD reduces the risk of longer term conduct disorder.

- *Epilepsy or epileptic syndromes*. Should be investigated and treated then ADHD symptoms reassessed.
- *Genetic/neurodevelopmental syndromes with behavioural phenotypes*. May need specialist medical genetic assessment if dysmorphic features.
- *Other psychiatric conditions*. Need specialist CAMHS assessment.
- *Child maltreatment*. Refer through Safeguarding Procedures.

Behavioural strategies

It is important in all families with a child who has ADHD that the whole family's behaviour management strategies are as effective as possible. Parental styles vary enormously and some families and individuals have more capacity to change than others. It will be helpful to explore with the carers how they respond to the 'target behaviours' and how effective this is. Enquiry should also be made as to whether they have had professional support with this in the past and how effective they considered that intervention to be. Some families are simply not able to engage with the available behaviour support services and these situations have to be dealt with pragmatically.

Community resources also vary enormously. In some areas there are good local schemes run under the auspices of Sure Start, Flying Start or by voluntary sector organizations such as Barnardos or the NSPCC. It is important to get to know what is available locally and how to tap into these resources. They can be very effective, particularly if they are delivered by members of the same community as the family, who share the same community culture and belief systems.

Schools and school health services will often have tried various interventions before the child ever presents to an ADHD clinic. Younger children may have had considerable support through their health visitor or Sure Start. If the child has a behaviour support plan at school, it may be helpful to look at the content and the set targets for the child. Sometimes they are unrealistic or inappropriate, such as one for a child with ADHD and Tourette disorder whose target is to 'sit still without shouting out for 5 min'. Not surprisingly, he will fail to achieve the target. Plans and targets must take into account the child's basic deficits in order to be effective. Schools may seek input from an educational psychologist or specialist teacher where needed, and in some cases an educational statement under the Education Act is needed.

Specialist non-NHS ADHD resources are available, although not universal. For example, some drug companies offer ADHD support schemes. There is also a range of web-based support which some families find helpful.

Specialist child psychology services are of particular value with families and children in more severe difficulty and can deliver more searching interventions in relation to management of 'difficult' behaviour. They are also invaluable in cases where there is concern about the emotional welfare of the child.

Specialist CAMHS will have a range of services, including specialist mental health assessments and a team comprising primary mental health workers, community psychiatric nurses and psychologists. The services available will vary from district to district, but they should include 'parenting skills' and anger management services. For some families, specialist family work

will be appropriate. The availability of specialist ADHD groups varies.

Medication

Indications

Medication for ADHD is indicated if impairment is severe or in milder cases where other interventions have been refused or have failed. Included here is a summary of the more relevant aspects of medication for ADHD, but it is not exhaustive and the prescribing clinician should be familiar with the full summary of product characteristics (SPC). These are usually available on the internet.

Cautions

Medication should be used with caution if there is doubt about diagnosis or in the presence of significant co-morbidity (including social co-morbidity). Caution is also needed in children with epilepsy or tics and those who are at risk of hypertension or cardiac arrhythmias.

Choice of starting medicine

Choice of medicine will depend on the clinical features and preferences of the child's carers. Older children may also have views on their treatment, which should be respected where possible. Stimulant and non-stimulant options are available. Most children will be started on a stimulant, usually methylphenidate, as their first-line drug of choice. The choice of treatment has been covered in a NICE guideline.³ Whichever medication is chosen, routine pre-treatment blood sampling is no longer recommended. The commonly used drugs all have comparable success rates and around four of five patients with ADHD will show useful improvement on first-line medical treatment. The decision should be based on a full discussion with the child and carers about the various options and their benefits and risks. Factors which may influence drug choice include:

- Whether evening or whole day cover is needed, in addition to controlling symptoms during school time;
- Whether there are major problems with appetite or sleep;
- Coexistence of Tourette, tics or seizure disorders;
- Views of the parent or child;
- Potential for misuse;
- Preferences arising from a discussion about side-effect profiles.

Stimulants are controlled drugs and need to be prescribed accordingly (guidance is contained in the *BNFc*). Atomoxetine is not a controlled drug.

Immediate-release methylphenidate

Immediate-release methylphenidate has the advantage of adjustability and short duration of effect. One dose typically is effective within 20–30 min and produces benefit in attention control for up to 3 h, so it needs to be given in two or three doses through the day. The number of doses depends on whether problems are experienced during the school day or extending into the evening. This means that a dose will have to be given in school and this will have to be negotiated with the teachers. The need to ask for the lunchtime dose is an unwelcome stigma for some children and this is one of the reasons why many children prefer a longer-acting preparation after the initial dose titration. The initial dose

of immediate-release methylphenidate will typically be 5 mg b.d., but this will need to be rapidly titrated upwards until a reasonable level of attention control is achieved. Titration can be fairly rapid as the effect of the drug is almost immediate. Some of this adjustment can be achieved by telephone consultations, but the child should be reassessed in clinic regularly and probably within 1 month of starting treatment. The necessary dose and duration of action are very variable and adjustment of dose is a clinical decision. Drug levels are not routinely monitored. Occasionally doses of up to 2.1 mg/kg/day or 90 mg total daily dose (or the equivalent as a long-acting preparation) are required, but at these doses the situation should be comprehensively reviewed.

Dexamfetamine

Dexamfetamine is broadly similar to methylphenidate in clinical terms but is less commonly used. The SPC gives a dose for children from 3 years old. The dose is approximately half that of methylphenidate (refer to *BNFc* or SPC for details). Some children may respond to dexamfetamine even if they do not respond to methylphenidate.

Longer-acting methylphenidate preparations

Concerta XL (Janssen), Equasym XL (UCB) and Medikinet XL (Flynn Pharma) are commonly used. The manufacturers suggest a typical duration of action of 12 h for Concerta XL and 8 h for Equasym XL and Medikinet XL. Concerta XL is in tablet form, whereas Equasym XL and Medikinet XL come in capsule form. Capsules may be opened and sprinkled (useful for children who cannot swallow tablets as there is no liquid preparation). The granules in Equasym XL and Medikinet XL capsules should not be chewed as they are formulated for slow release. In practice, duration of effect is variable but these preparations offer the advantage of not having to be taken in school, avoiding the stigma of having to ask for the medication at lunchtime. If converting from immediate-release methylphenidate to a long-acting preparation, the manufacturers claim that Equasym XL and Medikinet XL are dose-equivalent (e.g. 10 mg b.d. of IR-MPD equates to 20 mg of Equasym XL or Medikinet XL), whereas Concerta XL requires a slightly higher total daily dose (e.g. 5 mg t.d.s. of IR-MPD equates to 18 mg of Concerta XL). All forms of methylphenidate can be given on a 'school-day-only basis' and are suitable for 'treatment holidays' if desired.

All stimulants in common use are controlled drugs and must be prescribed in line with the guidelines in *BNFc*.

Non-stimulant alternative: atomoxetine

Atomoxetine (Strattera, Lilly) is said to be a selective noradrenaline (norepinephrine) reuptake inhibitor. It is very different from stimulants, particularly as it must be given regularly to have an effect and may take several weeks to achieve the desired effect. It therefore is not amenable to weekday-only administration or short drug holidays. Longer drug holidays are still possible, e.g. over the summer school holidays, but the medication should be restarted at least 1 week before term resumes. It is said to be as effective as methylphenidate as a first-line drug, though any drug used as second-line therapy after one medication has failed is less likely to be effective. In the UK, atomoxetine is often used as a second-line drug, although it may be used as first-line treatment if the child or their carers have a strong prejudice

against stimulants or if there are major concerns about weight or sleep, or if 24-h cover is needed. Atomoxetine comes in capsule form. With care the capsule can be opened and mixed with small amounts of food if necessary, but the contents can be irritant. It is sensible to consult the manufacturer do discuss particular circumstances if they arise. The starting dose of atomoxetine is 0.5 mg/kg once daily (timing is not crucial) for the first week followed by 1.2 mg/kg once daily. If response is poor after 6–8 weeks the dose may be increased to 1.8 mg/kg (check SPC). If switching from methylphenidate to atomoxetine treatment, it may be advisable to continue the methylphenidate for the first 1–2 weeks of atomoxetine therapy. The two drugs are compatible, although dual therapy is to be avoided. Exceptionally, patients on atomoxetine may ‘top up’ with methylphenidate but this causes us some concern and should lead to a search for a more effective longer-term strategy.

Third-line drugs

These include pemoline, clonidine, guanfacine, bupropion, modafinil, desipramine and imipramine, but these should only be used after tertiary assessment and are beyond the scope of this review. Antipsychotics such as risperidone are not effective for ADHD, although they may have a place in the treatment of some of the co-morbid conditions seen in children who also have ADHD.

Discussion with carers, including side effects

Carers should be informed that methylphenidate is a short-acting stimulant (many parents wrongly think it is a sedative) designed to improved attention control. They need to know about the more common stimulant side-effects and rarer idiosyncratic reactions. Appetite suppression is very common, so they should be told that the medicine should be given after meals unless obesity is an issue. Many children develop slight anxiety in the first few days after treatment is started or when the dose is increased. This often manifests as weepiness or clinginess but tends to pass after the first few days and is not a reason to stop treatment.

Other potential side-effects include tremor, palpitations, aggravation of nervous tics or Tourette disorder. Blood pressure rises are usually trivial but should be monitored. Weight tends to plateau and this may require treatment holidays periodically. Dietary advice and supplements may be needed for some children. Growth restriction is less common and, if it is noted, there will need to be a discussion with the carers about the risks and benefits of continuing treatment. In overdose, children become very ‘over-focused’, often picking at their clothes or fingers, becoming anxious and difficult to engage. Blood pressure will rise and there may be a tachycardia.

Idiosyncratic reactions to methylphenidate include rashes, which are uncommon and usually not serious, but do require cessation of medication, and rare cases of hepatitis or bone marrow suppression have been reported.

Atomoxetine may cause gastrointestinal symptoms, including stomach ache. Nausea and headache are also seen. Rare hepatic reactions have been reported. The association with suicidal ideation in adolescent patients should be discussed, although some express reservations about whether this is a side-effect or merely reflects the morbidity of the client group under treatment.

For a full list of contraindications and side-effects always refer to the data sheets or *BNFc*.

Parents will also need to know how to obtain repeat prescriptions. It is reasonable to ask the GP to do this but some decline. For these patients, a reliable and safe repeat prescribing system needs to be in place in secondary care.

Follow-up and duration of treatment

All children on medication should be followed up regularly. Initially there will be a need to titrate the dose (particularly with methylphenidate) and frequent contact may be needed, some of which may be by telephone or e-mail. Telephone and e-mail discussions should be documented in the child’s medical record. Most GPs do not possess the specialist skills to do this so this is usually done within secondary care, by paediatric services or CAMHS or jointly. Children who are stable on medication should be reviewed as a minimum every 6 months.

There is no limit to the duration of treatment. ADHD is probably a life-long condition but the impact of the problem will vary. As patients grow older they may learn better strategies for coping with their difficulty and the need for medication may be less. The greatest need for treatment is probably in the school years and many young people discontinue treatment of their own volition. For those who are still on treatment at school leaving age, there should be a transition plan. Increasingly, some adults with ADHD are recognizing their problem and requesting assessment and treatment. This is a relatively new phenomenon in the UK and services may or may not be available. The gap in services available in adult mental health in many areas needs to be addressed by health commissioners.

Treatment holidays

Given the short duration of action of methylphenidate, patients effectively experience a ‘treatment holiday’ every day when their medication wears off in the evening. Many families do not need medication at the weekend and intermittent dosing is perfectly acceptable. Longer breaks are indicated if side-effects, particularly poor weight gain, are an issue. When methylphenidate treatment is restarted the child may initially manage with a smaller dose, so re-titration is indicated.

Treatment holidays with atomoxetine require more planning as it will need to be restarted in good time to resume effect when needed.

Altering treatment dose or timing

Some titration of dose is usually needed, and patients who have been on methylphenidate for several months often notice a reduction in effect requiring an increase in dose of approximately 50%. The suggestions in Table 3 may be helpful.

Travel abroad

As methylphenidate is a controlled drug, patients will need a letter to take with them explaining their medication needs.

Sleep problems and night sedation

Many children with ADHD have disordered sleep at presentation. Stimulants may impair sleep or, paradoxically, treating the ADHD may promote better sleep routines. Parents should be taught effective sleep hygiene practices (most health visitors can

Suggestions for altering treatment dose or timing

Problem	Plan A	Plan B	Plan C	Notes
IR-MPD wearing off too soon	Increase dose	Change to long-acting preparation		Typical duration of effect 3 h
'Rebound' hyperactivity in evening 5–7 pm	Add IR-MPD in early evening 4 pm	Change to atomoxetine		Evening dose may shift rebound to later in day
Hyperactivity at bed time (check whether present before medication started)	Sleep hygiene strategies	Either omit or add evening dose of IR-MPD	Change to atomoxetine or add melatonin	Use of melatonin is helpful for some patients
LA-MPD wearing off too soon	Increased dose	Top up dose of IR-MPD after lunch or tea	Atomoxetine	
Short-lived anxiety after dose of MPD	Smaller more frequent doses	LA preparation	Atomoxetine	Check that medication is taken after food
Medication not working or making things worse	Reassess diagnosis	Change to alternative preparation	Stop medication and reassess behavioural methods	Consider tertiary referral
Poor weight gain (examine patient)	Check medication given after meals	Dietician review	Change to IR-MPD or atomoxetine	

IR-MPD, immediate-release methylphenidate; LA-MPD, longer-acting methylphenidate.

Table 3

do this). An evening dose of methylphenidate may help or may make things worse so a short trial of this may be indicated. If sleep disturbance is thought to be due to methylphenidate then a change to atomoxetine may help. Melatonin can be used and for some families is invaluable (ask the child's siblings!).

Treatment in younger children

Methylphenidate (like atomoxetine and dexamfetamine) is licensed for use for ADHD in children over 6 years of age. Rarely, and after specialist assessment, it may be used in younger children (sometimes as young as 3 years), but this must be subject to detailed consideration of risks and benefits and alternatives should have been fully explored before medication is considered. Consider referring these children for tertiary assessment. *BNFc* quotes doses of methylphenidate and dexamfetamine for children over 4 years.

Societal responses, obstacles and pitfalls

It is regrettable that some of the information in the public domain about ADHD is very misleading and misinformed. In some quarters there is considerable hostility towards the diagnosis, either total denial of the existence of ADHD as a discrete clinical entity or a focus on attributing blame, e.g. directed at 'bad parents', society in general, dysfunctional schools or overzealous doctors. It is not surprising that some parents feel beleaguered.

The best counter to this is to be as objective as possible about the impairment suffered by the child and the impact this is having on their social, educational and family life. Thorough assessment and careful diagnosis are essential. It must be emphasized that ADHD is an inherent neurodevelopmental disability and that without treatment the prognosis for many children is poor. Treatment, for many families, may be life-changing with substantial

improvement in measurable outcomes such as family relationships, educational outcomes and the risk of conduct disorder.

Of course, some parents have styles of behaviour management which are far from perfect. Some parents will have ADHD traits themselves which may cause some limitations. Being a parent of a child with ADHD is surely a great challenge, and some parents who are 'good enough' with an average child will not cope with a child with ADHD. It is important that the best available support is offered but sub-optimal parental styles are not necessarily a reason to withhold effective treatment for ADHD.

Unrealistic expectations should be addressed before treatment is started. Medication will improve attention control but will not necessarily stop children from being naughty or make them more intelligent. Sometimes treatment may actually improve a child's competence at challenging!

Many parents have an expectation that the Disability Living Allowance (DLA) or the equivalent will be awarded upon diagnosis of ADHD. This may be an unwelcome 'perverse incentive' in the ADHD clinic. Parents may need to be told that the DLA is awarded on the basis of the degree of impairment, not based on diagnosis. Always ask if the child has had their medication on the day of clinic. Information provided on DLA forms must be truthful and should reflect the child's abilities and performance whilst taking their prescribed treatment.

For some families the need for a diagnosis can over-step the mark somewhat, even to the extent of causing the child harm or placing them at risk. Deliberate fabrication of symptoms is the most extreme example and cases have been reported. If this is encountered a referral through Safeguarding Procedures is indicated.

Stimulants have a potential for misuse (as viewers of the TV soap 'Desperate Housewives' will have noted!). It is difficult for clinicians to guard against deception or to ensure that the drugs

they prescribe are actually consumed by their patient. Systems are needed to prevent the abuse of repeat prescription systems and, if there are substantial clinical inconsistencies leading the clinician to suspect misuse of a prescription drug, they should refuse to prescribe and consider making a Safeguarding referral. ♦

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Practice points

- ADHD is a common neurodevelopmental abnormality with discrete clinical features which causes significant morbidity
- Behavioural approaches are important in managing the condition and limiting impairment
- Medication is indicated for children who have severe impairment or for whom other strategies have not managed the problem to a satisfactory extent
- Medication is safe and effective for the vast majority of patients and reduces short and longer-term morbidity
- There are various co-morbidities which need careful assessment and may imply a less predictable response to medication
- Children are best seen in a specialized secondary care setting with access to paediatric and CAMHS services and a range of community services
- Some children will need to be referred for tertiary opinions
- NICE guidelines exist for this condition

Self-assessment

Case 1

A previously well, 11-year-old boy presented to the emergency department with a 4-day history of being unwell. His symptoms started with a headache and redness of the left eye. After 1 day he developed a fever of 40 °C together with an erythematous skin rash, a sore throat and generalized abdominal pain.

He was seen by his GP 3 days prior to admission, was diagnosed with tonsillitis and sinusitis, and was commenced on oral penicillin. He came to the emergency department today as his temperature was increasing, his rash had become more florid, and he had developed painful swallowing. He was drinking less, passing minimal amounts of urine and had three loose stools.

His initial observations are as follows: weight 48 kg, temperature 37.7 °C, heart rate 130 beats/min, blood pressure 87/33 mmHg, respiratory rate 40 breaths/min, capillary refill time less than 2 s, saturations 99% in air.

On examination he looks unwell, with bilateral red itchy eyes and red lips, and his tongue is very dry and cracked. He has bilateral tender cervical lymphadenopathy. His rash is erythematous, warm and blanching. He has bilateral enlarged tonsils with pus in the pharynx (Figure 1).



Figure 1 Rash found on examination.

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Initial investigations showed:

Haemoglobin	11.8 g/dl (9.6–14.8)
White blood cell count	$6.6 \times 10^9/L$ (5.0–14.0)
Neutrophil count	$5.79 \times 10^9/L$ (1.5–8.0)
Platelet count	$116 \times 10^9/L$ (200–420)
Sodium	125 mmol/L (135–145)
Potassium	3.2 mmol/L (3.5–5.0)
Urea	17.0 mmol/L (2.9–7.5)
Creatinine	113 mmol/L (44–108)
C-reactive protein	325 mg/L (0–5)

- What is the most likely diagnosis? Choose ONE answer ONLY from the following:
 - Kawasaki's disease
 - Tonsillitis and penicillin allergy
 - Toxic shock syndrome
 - Measles
 - Scarlet fever
- What is the most important initial management? Choose ONE answer ONLY from the following:
 - Intravenous immunoglobulin (IVIG)
 - Corticosteroids
 - Chlorpheniramine
 - Intravenous benzylpenicillin
 - Intravenous 0.9% saline fluid boluses

His condition remains resistant to the intervention above and he requires intubation and commencement of mechanical ventilation and transfer to the paediatric intensive care unit. His current observations include a heart rate of 150 beats/min and a mean blood pressure of 50 mmHg.

- Which of the following management options should be used next? Choose ONE answer ONLY from the following:
 - Furosemide
 - Aspirin
 - Inotropic support
 - Corticosteroids
 - Intravenous immunoglobulin (IVIG)

Case 2

A previously fit and well, 12-year-old girl is admitted to the paediatric ward. She has been unwell for 1 day with vomiting and abdominal pain. In the emergency department, she was seen by the SHO who referred her to the surgeons.

She is assessed on the paediatric ward and is dehydrated with dry mucous membranes and sunken eyes, and has generalized abdominal tenderness. The surgical team has suggested ordering an abdominal ultrasound. Unfortunately, it was not possible to obtain intravenous access in the Emergency department, but this is undertaken successfully on the ward.

Her initial observations are as follows: temperature 37.9°C, heart rate 120 beats/min with normal pulses, blood pressure 90/50 mmHg, respiratory rate 40 breaths/min, capillary refill time 3–4 s, saturations 95% in room air.

A venous blood gas taken when intravenous access was gained shows:

pH	7.18 (7.35–7.45)
pCO ₂	2.5 kPa (4.7–6.0)
pO ₂	5.3 kPa (8.0–10.0)
HCO ₃	9 mmol/L (22.0–26.0)
Base excess	–18 (–2.0 to + 2.0)
Sodium	134 mmol/L (135–145)
Potassium	4.5 mmol/L (3.5–5.0)
Glucose	***

- Which of the following investigations will help to confirm the diagnosis? Choose ONE answer ONLY from the following:
 - Ultrasound abdomen
 - Full blood count
 - Urine microscopy and culture
 - Stool culture
 - Urine dipstick
- What is the most appropriate initial fluid prescription? Choose ONE answer ONLY from the following:
 - IV 0.45% saline and 5% dextrose maintenance + deficit over 24 h
 - IV 0.45% saline and 5% dextrose with potassium as maintenance over 24 h
 - Trial of NG Dioralyte
 - 10 ml/kg normal saline bolus, followed by normal saline with potassium as maintenance + 10% deficit over 48 h
 - 10 ml/kg normal saline bolus followed by 0.45% saline and 5% dextrose maintenance + deficit over 48 h

Note deficit = % dehydration × body weight (kg)

Later that night you review the patient as she has been complaining of a headache. She has been given some paracetamol and by the time you arrive she has become drowsy. Her observations show the following: heart rate 70 beats/min, blood pressure 150/80 mmHg, capillary refill time less than 2 s and BM 10 mmol/L. You assess her Glasgow coma score (GCS) and it is 12/15.

- What should you do next? Choose ONE answer ONLY from the following:
 - Return to review her again in a couple of hours
 - A full neurological exam in the morning when she is more awake
 - CT head scan
 - Repeat blood gas
 - Treat raised intracranial pressure with mannitol or 3% saline

Case 3

A 9-month-old boy is brought to the Emergency department by his mother. He has a 2-day history of poor feeding and coryza.

Yesterday he only took three of his normal feeds. He was born at term with no complications.

On examination his heart rate is 140 beats/min, with a respiratory rate of 70 breaths/min and saturations of 92% in room air. He has moderate intercostal recession and, on auscultation, crepitations and wheeze throughout both lung fields. His temperature is 37.5 °C. He is pink, active and interacting with his mother.

- What is the most appropriate next step? Choose ONE answer ONLY from the following:
 - Capillary blood gas
 - Chest X-ray
 - Blood culture
 - Admit and start supportive treatment
 - Salbutamol nebulizer

You are called to review him later that evening as he has deteriorated, becoming more tachypnoeic with an increasing oxygen requirement. You take a capillary blood gas and organise a chest X-ray (Figure 2). A nasopharyngeal aspirate (NPA) is positive for respiratory syncytial virus (RSV).

His venous blood gas shows:

pH	7.30 (7.35–7.45)
PCO ₂	6.8 kPa (4.7–6.0)
Bicarbonate	25 mmol/L (22.0–26.0)
Base excess	3 (–2.0 to + 2.0)

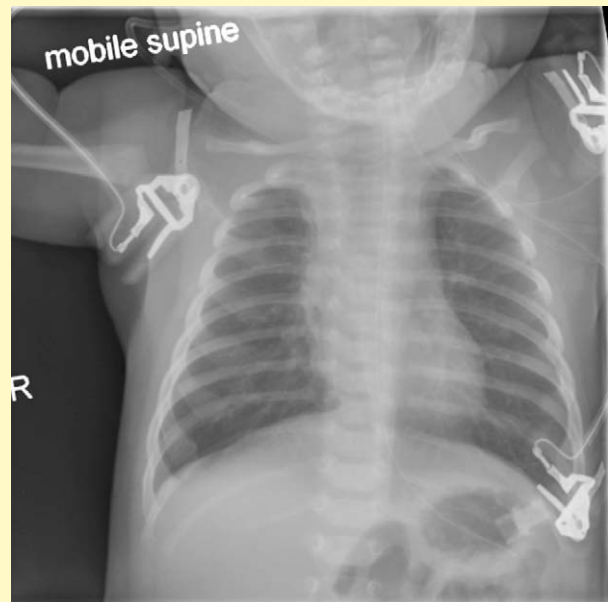


Figure 2 Chest X-ray of patient.

- Which of the following is the appropriate next step? Choose ONE answer ONLY from the following:
 - Atrovent nebulizer
 - Corticosteroids
 - Adrenaline nebulizer

- D. Stop feeds and commence intravenous fluids
- E. Salbutamol nebulizer

His nurse tells you that over the previous 3 h he has had three episodes of desaturation to 70% for 30 s, and required stimulation and increased oxygen to return to more than 95% in nasal cannulae oxygen.

3. Which other therapeutic option will be beneficial to this patient? Choose ONE answer ONLY from the following:
 - A. Intravenous antibiotics
 - B. Start nasal CPAP
 - C. Diuretics
 - D. Review in 1 h with repeat capillary blood gas
 - E. Arrange for intubation and ventilation

Case 4

A 7-year-old boy presents to the Emergency department with a 10-day history of fever, vomiting, mainly in the mornings, a headache which is not improving with regular ibuprofen, and he is more sleepy than normal. He has had no history of loss of consciousness. He has been feeling weak, has not been walking for 1 day and has started behaving strangely.

His initial observations are: temperature 36 °C, pulse 92 beats/min, mean blood pressure 80 mmHg, respiratory rate 30/min, saturations 99% in air, capillary refill time less than 2 s. His BM is 6.2 mmol/L and his urine dipstick is NAD.

He is alert, but moaning in pain with a GCS of 15/15. He has neck stiffness with a negative Kernig's sign. His cranial nerve examination is normal. Of note, on examining his reflexes, he has downgoing plantars. He has cervical lymphadenopathy and his tonsils are enlarged with an exudate present.

His initial venous blood gas is:

pH	7.52 (7.35–7.45)
pCO ₂	3.7 kPa (4.7–6.0)
HCO ₃	22.9 mmol/L (22.0–26.0)
BE	1.1 (–2.0 to +2.0)

Initial investigations showed the following:

Hb	12.2 g/dl (9.6–14.8)
White blood cell count	23.7 × 10 ⁹ /L (5.0–14.0)
Neutrophils	16 × 10 ⁹ /L (1.5–8.0)
Platelet count	555 × 10 ⁹ g/dl (200–420)
Sodium	130 mmol/L (135–145)
Potassium	3.4 mmol/L (3.5–5.0)
Urea	2.2 mmol/L (2.9–7.5)
Creatinine	61 mmol/L (44–108)
C-reactive protein	6.5 mg/L (0–5.0)

1. What is your management plan at this point? Choose ONE answer ONLY from the following:
 - A. Explain this is probably a viral infection, reassure and discharge home
 - B. CT head scan and lumbar puncture

- C. Discharge home with penicillin V for the tonsillitis
- D. Ask to return in 2 days if there is no improvement
- E. Admit to the ward for observation

While you are writing in your notes, before you have carried out your management plan, the nurse calls you over to review him. His vital signs are the following: temperature 37 °C, heart rate 68 beats/min, mean blood pressure 110 mmHg, respiratory rate 30–40 breaths/min with an irregular pattern, capillary refill time less than 2 s and saturations 92% in air. His GCS is 9.

2. What would you do next? Choose ONE answer ONLY from the following:
 - A. CT head scan and lumbar puncture
 - B. Give intravenous mannitol at a dose of 0.25–0.5 g/kg
 - C. Intubate and commence mechanical ventilation
 - D. Commence neurological observations every 15 min and review after 1 h
 - E. Fluid restriction

After an initial improvement, he has a further deterioration, is now making sterterous sounds and has developed focal seizures affecting his left leg. He is intubated and commenced on mechanical ventilation. His bloods are repeated and his serum sodium is 128 mmol/L.

3. What therapeutic manoeuvre will you institute next? Choose ONE answer ONLY from the following:
 - A. Give intravenous mannitol at a dose of 0.25–0.5 g/kg
 - B. Fluid restriction to 60% maintenance
 - C. Dose of intravenous 3% saline at a dose of 3 ml/kg
 - D. Dose of intravenous lorazepam at 100 µg/kg
 - E. Referral to neurosurgeon for placement of ICP bolt

Case 5

A 7-day-old baby presents to the emergency department with a 24-h history of poor feeding, and episodes of cyanosis. She was born at full-term by spontaneous vaginal delivery following an uncomplicated pregnancy with a birth weight of 3.2 kg. Her parents are non-consanguineous and she has a 2-year-old sibling who is well. She was discharged home on the second day of life, and has been breast feeding well.

On examination she is pale, and lethargic. Her weight is 3.5 kg, and she is tachypnoeic with a respiratory rate of 80 breaths/min. Her heart rate is 180 beats/min and her capillary refill time is 5 s. She has a liver palpable to 4 cm below the costal angle. It has been difficult to feel her femoral pulses and obtain a blood pressure in her lower limbs.

Intravenous access is gained and an initial venous blood gas shows:

pH	7.07 (7.35–7.45)
pCO ₂	3.7 kPa (4.7–6.0)
pO ₂	2.8 kPa
HCO ₃	10 mmol/L (22.0–26.0)
Base excess	–20 (–2.0 to +2.0)
Lactate	12 mmol/L (0–2.0)

- Which of the following best describes this blood gas? Choose ONE answer ONLY from the following:
 - Respiratory acidosis
 - Respiratory alkalosis
 - Metabolic alkalosis with respiratory compensation
 - Metabolic acidosis with respiratory compensation
 - Respiratory acidosis with metabolic compensation
- What is the likely diagnosis? Choose ONE answer ONLY from the following:
 - Bronchiolitis
 - Neonatal sepsis
 - Transposition of the great arteries
 - Coarctation of the aorta
 - Metabolic disorder

The baby deteriorates developing marked increased work of breathing followed by a prolonged apnoea and is fully resuscitated, with intravenous fluids and is intubated and commenced on mechanical ventilation.

- What therapy would be most valuable next? Choose ONE answer ONLY from the following:
 - Infusion of prostaglandin
 - Inhaled nitric oxide
 - Intravenous antibiotics
 - Inotropic support
 - Balloon atrial septostomy

Answers

Case 1

1. C

Toxic shock syndrome (TSS) is an acute, toxin-mediated febrile illness that rapidly leads to multiorgan failure, with serious morbidity and mortality. This patient meets the clinical criteria for diagnosis of TSS, i.e. a fever of at least 38.9 °C, a diffuse macular erythematous rash and hypotension. For diagnostic completion, toxin action on at least three systems must be demonstrated with either diarrhoea or vomiting, myalgia or raised creatinine kinase, mucous membrane hyperaemia, elevated concentrations of blood creatinine or urea, elevated transaminases, thrombocytopenia and confusion or drowsiness.

TSS is classically associated with the use of tampons, but it is well described in other circumstances. TSS is caused by *Staphylococcus aureus* and Group A β -haemolytic streptococcus. The bacterial toxins are known as 'superantigens' due to their ability to bypass the usual steps seen in the antigen-mediated immune response and directly to activate the immune system.

2. E

This child is shocked, which is apparent from his tachycardia, tachypnoea, hypotension (note the low diastolic pressure) and low urine output. Typically this is described as distributive shock and occurs when blood is redistributed

among organs. He is at risk of developing decompensated shock and requires urgent fluid resuscitation. The first-line fluid should be 0.9% saline and should be given as a fluid bolus of 20 ml/kg, maintaining close observations throughout.

3. C

This child requires inotropic support; the low diastolic blood pressure indicates peripheral vasodilation and an inotrope must be commenced.

IVIG (intravenous immunoglobulin) may be used for TSS and there is some evidence to suggest immunoglobulins directed against the toxins are an effective additional therapy, and useful when conventional therapies do not control the symptoms. It is thought that IVIG probably provides the antibodies to neutralize the antitoxin.

The use of corticosteroids in shock is controversial and should be discussed with a paediatric intensive care unit. As a therapy for TSS, they are not effective.

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Case 2

1. E

This child is dehydrated with abdominal pain and vomiting. In addition, she is tachypnoeic, has a metabolic acidosis and her glucose has not been recorded. Urine dipstick would confirm glycosuria and ketonuria, giving a diagnosis of diabetic ketoacidosis (DKA). A laboratory glucose will confirm this but it was not possible in the case described. DKA can sometimes present with features consistent with an acute abdomen. It is therefore important to dipstick the urine of any child who has abdominal pain or is vomiting.

2. D

She is 10% dehydrated, vomiting and acidotic, and requires IV fluids. In the management of DKA an initial fluid bolus may be given slowly if required followed by maintenance fluids. In order to correct the percentage of dehydration, the deficit of 10% is added to the fluid requirement and this should run over 48 h so as to not lead to any large fluid shifts and electrolyte changes. Maintenance fluids are always given initially as normal saline. Potassium may be required after initial resuscitation as insulin drives potassium uptake into cells; thus, serum electrolytes must be monitored regularly.

An intravenous insulin infusion should be commenced at 0.05–0.1 U/kg/h. The infusion should be titrated to aim for a fall of glucose no more than 5 mmol/L/h. This child must have hourly observations of her vital signs, including neurological observations. She should have ½ hourly to hourly blood glucose measurements and 4 hourly electrolytes. Regular monitoring and titration of insulin and fluids is essential in order to prevent deterioration.

3. E

This child has developed some signs of raised intracranial pressure, most likely due to cerebral oedema. This is evident with her headache, reduced GCS, increasing blood pressure and dropping heart rate. This must be treated as soon as possible with a hyperosmolar agent. Her blood glucose has dropped to 10 mmol/L. This rapid reduction in blood glucose and any accompanying fluid shifts may be associated with the development of intracranial hypertension in DKA.

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Wolfsdorf J, Craig ME, Daneman D, et al: ISPAD Clinical Practice Consensus Guidelines 2006–2007. Diabetic ketoacidosis. *Pediatr Diabetes* 2007;**8**:28–43.

Case 3

1. D

Bronchiolitis is the most common respiratory illness affecting children under the age of 2 years, with an incidence peaking in the first year of life. Its typical features start with symptoms of an upper airway viral infection, and over the following 4–6 days, the lower respiratory tract becomes affected with cough, tachypnoea, hyperinflation, widespread crackles and wheeze. In November 2006 the Scottish Intercollegiate Guidelines Network (SIGN) published an evidence-based guideline on the management of bronchiolitis. For the hospital management of bronchiolitis, it recommends that all infants with oxygen saturation $\leq 92\%$ require inpatient care and that infants with oxygen saturations more than 94% in room air may be considered for discharge. Blood culture and chest X-ray are not necessary. Blood gas measurement is only required in severe cases.

2. D

As this child has become more distressed, it is most appropriate to stop gastric feeds and commence intravenous fluids. The use of nebulized agents has no scientifically defined recommendation; however, in the clinical setting,

it may be useful to administer these agents at least on a trial basis.

3. B

The use of CPAP is appropriate where there is a respiratory deterioration and apnoeas. If there is no benefit from CPAP, then intubation and mechanical ventilation are indicated.

FURTHER READING

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Case 4

1. B

This child has signs and symptoms consistent with a meningococcal infection. Initially the child is stable and at this point it is advisable to perform a CT head to rule out a space-occupying lesion, e.g. a cerebral abscess, and if appropriate to proceed to perform a lumbar puncture. A normal CT brain scan does not rule out raised intracranial pressure. This is safe to do as his neurological examination is normal and there are no other contraindications.

2. B

He has developed signs of raised intracranial pressure with a decreased level of consciousness, raised blood pressure and bradycardia. At this point the lumbar puncture is not indicated because the risk of cerebral herniation is high.

Hyperosmolar therapy is used for treating raised intracranial pressure in the acute setting. The agents used for hyperosmolar therapy are mannitol and 3% saline. Mannitol acts by reducing blood viscosity and therefore blood vessel diameter – where there is intact cerebral autoregulation. Mannitol also acts by its osmotic effect. Although no studies on mannitol have been carried out in children, it is used extensively. Hypertonic saline also acts to increase the hypertonicity of cells, and is becoming incorporated into the acute management of intracranial hypertension.

3. D

He has developed focal seizures that must be controlled as soon as possible. The algorithm for the management of seizures must be followed. The seizures may be due to intracranial hypertension and treatment can be instituted for this.

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Case 5

1. D

This baby has developed a metabolic acidosis with respiratory compensation.

2. D

3. A

Coarctation of the aorta presenting in the neonatal period usually has an acute onset of obstruction to systemic blood flow, leading to left ventricular failure and cardiovascular collapse. A patent ductus arteriosus (PDA) allows blood to pass from the right ventricle to the descending aorta, and when the PDA closes, this leads to acute cardiovascular collapse. This can lead to a baby presenting with severe shock, metabolic

acidosis and end-organ ischaemia. Other left-sided obstructive lesions, including hypoplastic left heart syndrome, may present in a similar way. The baby must be resuscitated on presentation, and for any duct-dependent cardiac lesion this includes an infusion of Prostaglandin in order to open up the duct to allow blood to flow into the descending aorta.

These babies must be reviewed by a paediatric cardiologist as soon as possible, in order to perform an echocardiogram to confirm and review the anatomical diagnosis.

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Which inotrope?

Fauzia Paize

Stephen D Playfor

Abstract

Critically ill children with shock frequently require the administration of inotropic and vasoactive agents. The appropriate choice of inotropic agent in these children forms only part of their overall management. In most cases children requiring inotropes should already have received aggressive fluid resuscitation and prompt tracheal intubation and mechanical ventilation will be indicated in the majority of cases. The first-line inotrope for children with shock and hypotension is dopamine. Dopamine should be administered centrally or via the intraosseous route. In patients resistant to fluid therapy and dopamine secondary agents should be administered; adrenaline for 'cold shock' and noradrenaline for 'warm shock'. Simple clinical and therapeutic endpoints should be used as surrogate markers of cardiac output in order to monitor progress and response to treatment. Children requiring inotropic or vasoactive agents should be reassessed frequently as the cardiovascular profile of children with shock frequently changes particularly during the early phases of their illness.

Keywords inotrope; paediatrics; sepsis; shock

Introduction

Critically ill children with shock frequently require the administration of inotropic and vasoactive agents; hence the question of which inotrope to administer in a particular clinical situation is a frequently asked question in clinical practice.

Physiological principles

Shock is a state of circulatory dysfunction where the oxygen and nutrient demands of the tissues cannot be met by the circulation. Oxygen delivery to the tissues is determined by the oxygen content of the blood and the cardiac output.

$$\text{Oxygen delivery (DO}_2\text{)} = \text{oxygen content} \times \text{cardiac output} \\ (\text{stroke volume} \times \text{heart rate})$$

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Stroke volume is in turn determined by cardiac preload (filling), myocardial contractility and cardiac afterload: arterial blood pressure is determined by the cardiac output and the systemic vascular resistance.

Inotropic and vasoactive agents are primarily indicated in situations where shock has developed as a result of impaired myocardial contractility, or because of dysfunction of the peripheral vascular bed, such as increased capillary permeability or reduced systemic vascular resistance.

Clinical situations where inotropes would commonly be administered include septic shock, cardiogenic shock and distributive shock. In septic shock the release of inflammatory mediators results in vascular endothelial dysfunction and capillary leak; furthermore, there is direct myocardial impairment as a result of inflammatory mediators such as interleukin-6. Similar physiological changes may be seen in situations associated with a marked systemic inflammatory response syndrome, such as following cardiopulmonary bypass. Cardiogenic shock may be the result of myocarditis or cardiomyopathy, whilst distributive shock can be seen in anaphylaxis or as a result of spinal cord injury.

General management of the critically ill child with shock

It is important to remember that appropriate inotrope selection is only one facet of the effective management of the critically ill child with shock. This process begins with the recognition of the child as being seriously ill. When a child is diagnosed as being in shock, their airway and breathing should be assessed and supported as necessary, and oxygen should be applied. Initial fluid resuscitation should be aggressive with infusion of crystalloid or colloid boluses of 20 ml/kg, repeated as necessary and titrated to clinical markers of cardiac output, including heart rate, capillary refill and level of consciousness. Children not responding to 60 ml/kg of initial fluid resuscitation have 'fluid refractory shock' and require intubation, mechanical ventilation and the administration of inotropic agents.

Initial selection of inotropic agents

The Surviving Sepsis Campaign international guidelines for the management of severe sepsis and septic shock were published in 2008 and recommend *dopamine* as the first choice of inotrope to support the paediatric patient with hypotension refractory to fluid resuscitation.

The administration of dobutamine as an initial inotrope should be reserved for patients who still have features of low cardiac output following fluid resuscitation, but who have normal blood pressure and clinical evidence of elevated systemic vascular resistance (prolonged capillary refill, cool extremities and a widened core-peripheral temperature gap).

These inotropes should ideally be administered through a central venous catheter, but may also be infused through an intraosseous line. Powered intraosseous access devices such as the EZ-IO® device allow secure vascular access to be obtained within 60 s and facilitate the administration of inotropes in the emergency department or general paediatric areas. Patients requiring inotropic support should have an indwelling arterial and urinary catheter sited, and should be referred to a paediatric intensive care unit (PICU).

Children not responding to this level of therapy have 'fluid refractory-dopamine resistant shock' and require the administration of additional inotropic agents.

Subsequent selection of inotropes and vasoactive agents

The subsequent choice of inotropes and vasoactive agents is determined by clinical examination and estimation of the cardiac output. In most cases this involves the use of physical examination and therapeutic endpoints, which can be applied in any clinical setting, although within the PICU various cardiac output monitors may also be employed.

Therapeutic endpoints in the management of shock should include normalization of the heart rate, a capillary refill time of less than 2 s, normal volume pulses with no differential between peripheral and central pulses, warm extremities with a modest core-peripheral temperature gap, urine output more than 1 ml/kg/h and normal mental status. Blood gas estimation should show a decreasing lactate and an improving base deficit. Central venous pressure should be maintained at 8–12 mmHg.

Central venous (ScvO₂) and mixed venous (SvO₂) oxygen saturations are measurements of the relationship between oxygen consumption and oxygen delivery in the body, and are easily measured therapeutic endpoints in the management of shock. Normal values for ScvO₂ will be slightly higher than the SvO₂ as blood has not mixed with the venous blood from the coronary sinus. In shock the therapeutic endpoint for ScvO₂ should be $\geq 70\%$ and $\geq 65\%$ for the SvO₂.

In managing the child with 'fluid refractory-dopamine resistant shock' typical choices for a 'second-line' inotrope would be *adrenaline* (epinephrine) for the child with low blood pressure and high systemic vascular resistance (so-called 'cold shock') or *noradrenaline* (norepinephrine) for the child with low blood pressure and low systemic vascular resistance (so-called 'warm shock').

Children with a persistent low cardiac output state with high systemic vascular resistance despite fluid resuscitation and inotropic support may benefit from vasodilator or inodilator therapy, particularly if the arterial blood pressure is relatively well maintained. A typical choice in this circumstance would be a type III phosphodiesterase inhibitor such as *milrinone*.

In cases where there is extremely low systemic vascular resistance, resistant to the administration of noradrenaline, *vasopressin* use has been described in a number of case reports with some success. There is, however, limited experience in the use of vasopressin in paediatric sepsis and this agent should be used with caution.

Within the PICU, cardiac output monitoring may be available to allow measurement of the cardiac index and the calculation of other parameters such as the systemic vascular resistance. These devices have become more reliable and less invasive over time; pulmonary artery catheters are now rarely used in this setting, and have largely been superseded by less invasive systems such as PiCCO, LiDCO and the more recently developed PRAM and FloTrac devices. When available, therapeutic endpoints would be a cardiac index more than 3.3 and less than 6.0 Litres/min/m², with normal coronary perfusion pressure (mean arterial pressure minus central venous pressure) for age.

Frequent reassessment of children with shock is necessary as the haemodynamic profile of critically ill children frequently changes, particularly during the early phase of their illness.

Adjunctive therapy

Intravenous infusions of *calcium* may transiently increase arterial blood pressure; they are not recommended for routine use in shock but may be of benefit in patients who have a low blood ionized calcium level.

Administration of *glucocorticoids* to healthy subjects increases cardiac index and systemic vascular resistance. Glucocorticoids may also reduce catecholamine requirements in some patients with significant haemodynamic instability and hydrocortisone therapy may be considered for use in children with catecholamine resistance and suspected or proven adrenal insufficiency.

There is some suggestion that *triiodothyronine* (T₃) supplementation may increase cardiac output in some clinical circumstances, although there is insufficient evidence to support its routine use.

Receptors for inotropes and vasoactive agents

The effects of dopamine, dobutamine, adrenaline and noradrenaline are mediated through adrenergic receptors, whilst dopamine also acts at dopamine receptors.

α adrenergic receptors

These are either pre- or post-synaptic. Cardiac and vascular pre-synaptic α_2 receptors are activated by noradrenaline released by sympathetic nerves and mediate negative feedback inhibition of further noradrenaline release. The stimulation of postsynaptic cardiac α_1 receptors causes an increase in contractility without an increase in heart rate. The stimulation of postsynaptic α_1 and α_2 receptors in peripheral vessels produces vasoconstriction.

β adrenergic receptors

These are either β_1 or β_2 . Postsynaptic β_1 receptors are predominantly cardiac adrenergic receptors; stimulation of these causes an increase in heart rate and the positive inotropy. The stimulation of vascular postsynaptic β_2 receptors causes vasodilatation.

Dopamine receptors

There are five subtypes of dopamine receptors which are grouped into two families: the D₁-like family (excitatory) and the D₂-like family (inhibitory). Peripheral D₁ receptors mediate renal, coronary and mesenteric arterial vasodilatation; they also have a natriuretic response. Presynaptic D₂ receptor stimulation inhibits noradrenaline release from sympathetic nerve endings.

Pharmacological considerations

Dopamine

Dopamine is a naturally occurring endogenous catecholamine and a precursor of noradrenaline and adrenaline. The primary pharmacodynamic effects of dopamine include inotropy, chronotropy, vasoconstriction, and renal and splanchnic vasodilatation. The normal infusion rate is 5–20 $\mu\text{g/kg/min}$.

Dobutamine

Dobutamine is a synthetic catecholamine with the same basic structure as dopamine. It is an inodilator with β_1 and α_1 stimulation

but has no α agonistic effect. The normal infusion rate is 5–20 $\mu\text{g}/\text{kg}/\text{min}$.

Adrenaline

Adrenaline is a potent endogenous catecholamine which stimulates both α and β adrenoreceptors, with β_1 and β_2 effects being predominant at lower doses. Stroke volume and cardiac index increase in a dose-dependent manner, oxygen consumption is increased and the heart rate increases. The normal infusion rate is 0.05–2.0 $\mu\text{g}/\text{kg}/\text{min}$.

Noradrenaline

Noradrenaline is an endogenous catecholamine which has powerful α agonist and β_1 activity similar to adrenaline, but with little β_2 activity. Standard therapeutic doses result in significant increases in systemic vascular resistance with some inotropy. The normal infusion rate is 0.05–2.0 $\mu\text{g}/\text{kg}/\text{min}$.

Milrinone

Milrinone is a type III phosphodiesterase (PDE III) which acts as an inodilator. It exerts inotropic action by inhibiting the breakdown of cAMP, hence elevating cellular cAMP, which in turn activates cAMP-dependent protein kinases with a resultant increase in the transsarcolemmal influx of calcium and the rate of calcium uptake by the sarcoplasmic reticulum. Milrinone is predominantly excreted in urine so doses may need to be adjusted

if there is deteriorating renal function to avoid toxicity. The infusion dose is 0.25–0.75 $\mu\text{g}/\text{kg}/\text{min}$. ◆

Practice points

- Aggressive resuscitation – choosing the most appropriate inotrope is only part of the process of managing the critically ill child. Children requiring inotropes should already have received aggressive fluid resuscitation, and prompt tracheal intubation and mechanical ventilation should be established in the majority of cases
- Dopamine – the first-line inotrope for children with shock and hypotension should be dopamine. This should be administered centrally or via the intraosseous route
- Second-line inotropes – administer adrenaline for ‘cold shock’ and noradrenaline for ‘warm shock’
- Therapeutic endpoints – use simple clinical and therapeutic endpoints as surrogate markers of cardiac output in order to monitor progress and response to treatment
- Reassess frequently – the cardiovascular profile of children with shock frequently changes during the early phases of their illness. Reassess these children frequently and adjust their treatment as necessary

Erratum to: The changing epidemiology of parapneumonic empyema in children. [*Paediatrics and Child Health* 2008; 18 (11): 513–518]. Spencer DA and Cliff D

The publishers and the authors wish to apologise to readers for errors that have occurred in the above review.

Page 514, left hand column, line 6 from top

“The incidence of PPE has increased dramatically in children in the UK and other **predominantly** western countries....”

Page 514, left hand column

The first paragraph of text under the heading “**Burden of disease**” should be deleted as the authors believe that the statement cannot be adequately supported with evidence.

Page 514, Table 1

Please refer to the revised table below which contains some important corrections.

Page 514, right hand column

The last sentence in the paragraph headed “**Clinical diagnosis of PPE**” should include a reference citation as follows:

“Computed tomography (CT) has no part to play in routine management.¹⁰”

Page 515, left hand column

The first sentence of paragraph 2 under the heading “**Morbidity of PPE**” contains changes to the reference citations as follows:

“PPE causes significant acute morbidity⁹ although death is uncommon in previously healthy children living in western countries.”

Page 515, right hand column

The first paragraph of text under the heading “**Why has there been an increase in incidence of PPE?**” contains three separate citations to reference 14; these actually refer to reference 15.

Page 516, right hand column

The final paragraph of text under the heading “**Summary and prospects for prevention**” contains the citation to reference 20, which should be deleted.

Page 516, Table 2

Please refer to the revised table on the next page which contains some important corrections.

Page 516, caption to Fig 4

The caption should read:

“**Figure 4.** Serotypes of *Streptococcus pneumoniae* isolates responsible for parapneumonic empyema: US Study. Adapted with permission from Tan *et al.*²⁷”

Page 517, Table 3

The heading for the table should read

“Possible risk factors associated with increase in incidence of empyema^{15, 40}”

Increasing worldwide incidence of complicated pneumonia, parapneumonic empyema and/or pleural effusions

Country	Reference	Age group	Disease	Years	Incidence
USA (Utah)	Byington <i>et al.</i> 2002 ¹⁵	<19 years	PPE	1994	1 per 100,000
				1999	5 per 100,000
USA (Alaska)	Singleton <i>et al.</i> 2007 ²⁰	<5 years	PPE	1995–2000	2% cases†
				2004–2006	13% cases†
France (Grenoble)	Desrumaux <i>et al.</i> 2007 ¹⁶	Children*	Pneumonia complicated by empyema or lung abscesses	1995	0.5 per 100,000
				2003	13 per 100,000
Spain (Barcelona)	Calbo <i>et al.</i> 2006 ²¹	≤5 years	PPE	1999–2001	1.7 per 100,000
				2002–2004	8.5 per 100,000
Spain (Barcelona)	Muñoz-Almagro <i>et al.</i> 2008 ¹¹	<2 years	Pneumonia with empyema	1997–2001	2.2 per 100,000
				2002–2006	9.2 per 100,000
		2–4 years		1997–2001	1.5 per 100,000
				2002–2006	9.2 per 100,000
		5–17 years		1997–2001	0.5 per 100,000
				2002–2006	1.3 per 100,000
Spain (Madrid)	Deiros Bronte <i>et al.</i> 2006 ¹⁸	<15 years	Parapneumonic effusions		18 per 100,000
					43 per 100,000
UK	Gupta & Crowley 2006 ¹⁹	<15 years	Pyothorax (empyema, pneumoempyema and lung abscesses)	1995/6	14 per million
				2002/3	26 per million
Taiwan	Hsieh <i>et al.</i> 2004 ¹⁷	<15 years	Empyema and/or necrotising pneumonia	1995	25% cases†
				2002	70% cases†

*Age groups not defined. †Proportion of pneumococcal pneumonia cases that had PPE and/or necrotising pneumonia. PPE, parapneumonic empyema.

Table 1

DOI of original article: 10.1016/j.paed.2008.07.013

Principal bacterial pathogens causing childhood empyema

Reference	Country	<i>Streptococcus pneumoniae</i> (% cases)	<i>Streptococcus pyogenes</i> (% cases)	<i>Staphylococcus aureus</i> (% cases)
Le Monnier <i>et al.</i> 2006 ²⁵	France	51	9	8
Saglani <i>et al.</i> 2005 ²⁶	UK	44	13	9
Eastham <i>et al.</i> 2004 ³⁰	UK	66	2	2
Hardie <i>et al.</i> 1996 ²⁸	USA	40	No data	0
Buckingham <i>et al.</i> 2003 ³¹	USA	41	7	9
Hardie <i>et al.</i> 1998 ³²	USA	36	0	2

Table 2

Page 517, left hand column

The last two sentences of the text contain some changes to reference citations as follows:

“The pneumococcal, *H. influenzae* protein D conjugate vaccine (PHiD-CV) — which is in development and active against 10-valent polysaccharide serotypes (1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F)⁴² — and also PCV13 currently in development, offer additional coverage against three major serotypes compared with

PCV7. They may also confer a benefit in the prevention of severe pneumonia and empyema.”

Page 517, Reference 4

The reference should read:

4. Aboud FC, Verghese AC. Evart Ambrose Graham, empyema and the dawn of clinical understanding of negative intrapleural pressure. *Clin Infect Dis* 2002; **34**: 198–203. ◆