54 Mechanical Ventilation in Infection, Sepsis and Organ Failure

Andrew C. Argent and Niranjan “Tex” Kissoon

Educational Aims

• Consider an approach to ventilation in patients with sepsis of all kinds.
• Discuss some of the possible modes of ventilatory support, with particular attention to their potential use in patients with sepsis or organ failure.
• Consider anaesthesia for initiation of invasive ventilation in patients with sepsis.
• Define the goals of ventilation in patients with severe sepsis or organ failure.
• Review the cardiovascular implications of ventilatory support in patients with sepsis.
• Consider processes to minimize lung damage during ventilation.
• Consider specific infections and some of the implications for ventilation.
• Briefly address issues of infection control.

54.1 Introduction

Each day thousands of children across the world die as a result of infection. Sepsis, severe sepsis and septic shock represent a continuum of increasing severity for which present definitions are not wholly satisfactory (Levy et al. 2003; Brilli and Goldstein 2005). The term sepsis refers to the presence of an infection caused by a microbe that invades tissue, fluid or a body cavity that is normally sterile, plus the presence of clinical and/or laboratory evidence of the systemic inflammatory response syndrome (SIRS, temperature or leucocyte abnormalities and abnormal vital signs) (Goldstein et al. 2005). When sepsis is complicated by multi-organ failure, it is regarded as severe, while septic shock is diagnosed when sepsis coexists with a state of acute circulatory failure (Levy et al. 2003).

Sepsis may be related to a wide variety of different microorganisms (Goldstein et al. 2005) (including bacteria, viruses, protozoa, rickettsiae and fungi) with many different toxins and pathogenic mechanisms. In addition, the clinical features of infection in a patient may vary due to a variety of factors including the genetic predisposition (Opal 2007); infective dose, route of infection and virulence factors of the particularly organism; possible co-infections; and underlying illness, nutritional status, medication; and the organs affected by the infection (and responses) (Opal 2005).

Thus septic patients who require ventilation make up a very broad spectrum of contexts and specific situations. The indications for and the goals of ventilation may therefore vary considerably in patients (Table 54.1).
| Category | Features | Criteria |
|----------|----------|----------|
| **Systemic inflammatory response syndrome (SIRS)** | The presence of at least two of the following four criteria, one of which must be abnormal temperature or leucocyte count | Core temperature of >38.5 °C or <36 °C. Tachycardia, defined as a mean heart rate >2 SD above normal for age in the absence of external stimulus, chronic drugs or painful stimuli or otherwise unexplained persistent elevation over a 0.5- to 4-h time period, OR, for children <1 year old, bradycardia, defined as a mean heart rate <10th percentile for age in the absence of external vagal stimulus, β-blocker drugs or congenital heart disease or otherwise unexplained persistent depression over a 0.5-h time period. Mean respiratory rate >2 SD above normal for age or mechanical ventilation for an acute process not related to underlying neuromuscular disease or general anaesthesia. Leucocyte count elevated or depressed for age (not secondary to chemotherapy-induced leucopenia) or >10 % immature neutrophils. |
| Infection | A suspected or proven (by positive culture, tissue stain or polymerase chain reaction test) infection caused by any pathogen OR a clinical syndrome associated with a high probability of infection | Evidence of infection includes positive findings on clinical exam, imaging or laboratory tests (e.g. white blood cells in a normally sterile body fluid, perforated viscus, chest radiograph consistent with pneumonia, petechial or purpuric rash or purpura fulminans). |
| Sepsis | SIRS in the presence of or as a result of suspected or proven infection | |
| Severe sepsis | Sepsis plus one of the following: cardiovascular organ dysfunction OR acute respiratory distress syndrome OR two or more other organ dysfunctions | *Cardiovascular dysfunction* See below under septic shock  
*Respiratory*  
\( \text{PaO}_2/\text{FiO}_2 < 300 \) in the absence of cyanotic heart disease or pre-existing lung disease  
OR  
\( \text{PaCO}_2 > 65 \) Torr or 20 mmHg over baseline \( \text{PaCO}_2 \)  
OR  
Proven need or >50 % \( \text{FiO}_2 \) to maintain saturation >92 %  
OR  
Need for nonelective invasive or noninvasive mechanical ventilation  
*Neurologic*  
Glasgow Coma Score <11  
OR  
Acute change in mental status with a decrease in Glasgow Coma Score >3 points from abnormal baseline  
*Haematologic*  
Platelet count <80,000/mm³ or a decline of 50 % in platelet count from highest value recorded over the past 3 days (for chronic haematology/oncology patients)  
OR  
International normalized ratio >2  
*Renal*  
Serum creatinine >2 times upper limit of normal for age or twofold increase in baseline creatinine  
*Hepatic*  
Total bilirubin >4 mg/dL (not applicable for newborn)  
OR  
ALT 2 times upper limit of normal for age |
The Nature of Ventilatory Support

Strategies for assisting ventilation include endotracheal intubation and positive pressure ventilation and recently several other modes including noninvasive techniques. Ventilatory support using high-flow humidified nasal oxygen has been introduced into neonatal practice for respiratory support. There are limited reports of its use in older children with respiratory distress (Spentzas et al. 2009; McGinley et al. 2009). There are a number of commercial systems available. There is considerable variability in the pressures and flows delivered to infants with these systems (Dani et al. 2009; Lampland et al. 2009), and it is suggested that pressure limitation devices should be incorporated (Lampland et al. 2009). More research is required before these can be recommended for respiratory support in children (Randolph 2009) with acute respiratory distress.

Noninvasive ventilation has been attempted in children with acute respiratory failure due to a wide variety of conditions (Teague 2005) including neuromuscular conditions (Katz et al. 2004; Reddy et al. 2004; Hartmann et al. 1994), asthma (Haggenmacher et al. 2005; Ram et al. 2005) as well as acute respiratory failure due to infections (Prado et al. 2005; Piastra et al. 2004; Fortenberry et al. 1995).

After an initial report of nCPAP in an infant with apnoea related to RSV infection (McNamara and Sullivan 1997), Thia et al. (2008) demonstrated that nCPAP administered to infants with bronchiolitis and hypercapnia was associated with significant improvement.

A report on 14 patients from Chile (Prado et al. 2005) showed that nCPAP or BiPAP administered via nasal mask in acute respiratory failure due to infection was associated with significant improvement and that most children did not need invasive ventilation.

A recent Cochrane review of negative pressure ventilation in acute respiratory failure (Shah et al. 2005) concluded that there was not enough evidence available to make a recommendation as to its clinical applicability.

Thus it may be possible to use conventional or noninvasive (including nCPAP, BiPAP and mask) ventilation in children with acute respiratory failure related to infection. Unfortunately firm recommendations cannot be made until challenges in terms of masks (including fit), indications and techniques are elucidated (Teague 2005; Loh et al. 2007) and proposed predictors of success (Bernet et al. 2005) confirmed.

### Table 54.1 (continued)

| Category         | Features                                      | Criteria                                                                 |
|------------------|-----------------------------------------------|--------------------------------------------------------------------------|
| Septic shock     | Sepsis and cardiovascular organ dysfunction as defined | Despite administration of isotonic intravenous fluid bolus ≥40 ml/kg in 1 h |
|                  |                                               | Decrease in BP (hypotension) <5th percentile for age or systolic BP <2 SD below normal for age OR |
|                  |                                               | Need for vasoactive drug to maintain BP in normal range (dopamine >5 μg/kg/min or dobutamine, epinephrine or norepinephrine at any dose) OR |
|                  |                                               | Two of the following: Unexplained metabolic acidosis: base deficit >5.0 mEq/l Increased arterial lactate >2 times upper limit of normal Oliguria: urine output <0.5 ml/kg/h Prolonged capillary refill >5 s Core to peripheral temperature gap >3 °C |

From Goldstein et al. (2005)
54.3 Initiation of Ventilation

Anaesthesia for endotracheal intubation for conventional ventilation is essential, but there is considerable controversy regarding the optimal agents for anaesthesia in acute sepsis (Zelicof-Paul et al. 2005). Selection of appropriate agents will depend on experience and training.

54.4 Drugs for Intubation

Etomidate has been used in a number of studies, but there remains considerable concern regarding possible adrenal suppression following its use in sepsis (Zed et al. 2006; Zuckerbraun et al. 2006). It does however create favourable conditions for intubation (Zelicof-Paul et al. 2005) and is less likely to cause hypotension than agents such as midazolam (Choi et al. 2004).

Ketamine has been used extensively in many settings with a very low complication rate (Melendez and Bachur 2009; Jankiewicz and Nowakowski 1991) and is an agent of choice in many emergencies, while propofol and thiopentone have been used with some success.

54.4.1 Use of Atropine

There is a theoretical benefit for giving atropine when manipulating the airway of infants under 1 year of age due to their disproportionate predominance in vagal tone coupled with a relatively greater dependency on HR for cardiac output (Rothrock and Pagane 2005). However recent evidence suggests that it may be unnecessary (Brown et al. 2008) when ketamine alone is used for anaesthesia. Most bradycardias are due to hypoxia or are a transient vagally mediated reflex response that resolves spontaneously. In special circumstances, such as infants less than 1 year of age, atropine is still considered an option by some practitioners especially prior to a second or repeat dose of succinylcholine.

54.4.2 Use of Paralytic Agents

The choice of agent for paralysis in intubation under emergency conditions remains controversial. Recent reviews of the adult literature have concluded that there is no benefit to rocuronium and that succinylcholine remains the safest agent (Perry et al. 2008). In the 1990s reviews of the use of succinylcholine vs. rocuronium concluded that succinylcholine remained the recommended choice although this was essentially a matter of personal preference (Robinson et al. 1996; Weir 1997). There have been concerns about the possibility of hyperkaemic cardiac arrest in the setting of undiagnosed neuromuscular disease. A recent paediatric review (Ching and Baum 2009) has concluded that rocuronium may be a safer agent for use in emergency intubation in children.

A significant concern that has been raised recently (Kendrick et al. 2009) is that the duration of action of agents such as rocuronium or atracurium is significantly longer than that of etomidate. Thus patients who are intubated using the combinations of etomidate and rocuronium or atracurium should receive sedation after intubation to avoid the possibility of awareness while paralysed.

54.5 The Goals of Ventilation

Mechanical ventilation in respiratory failure has been one of the core functions of intensive care since the earliest days of the speciality (Grenvik and Pinsky 2009). The goals of mechanical ventilation have primarily been focused on the maintenance of acceptable blood gases in patients with failure of the respiratory system, but there is also a considerable body of literature related to cardiopulmonary interactions and the effect of mechanical ventilation on cardiovascular function (Bronicki and Anas 2009).

Essentially the goals of ventilation in sepsis and organ failure could be summarized as:

- Maintenance of blood gas values that are appropriate to the overall management of the patient (taking into account the effects of sepsis of all organ systems)
- Optimization of cardiovascular function
- Minimizing damage to the lungs and the respiratory system
- Minimizing deleterious effects on other organ systems
The priorities of ventilation in sepsis, from the immediate resuscitation at the time of presentation through the recovery phases of the illness, may differ as the physiology changes. Thus acceptable goals will depend on the stage of the illness.

### 54.5.1 Acceptable Blood Gas Values

It has been generally accepted that mechanical ventilation in patients with respiratory disease should not always be aimed at the maintenance of normal blood gas values, and recent reviews refer to both permissive hypoxaemia (Cheifetz and Hamel 2006) and hypercapnia (Hickling 2002) and even to therapeutic hypercapnia (Laffey et al. 2000, 2004a; Kavanagh and Laffey 2006).

#### 54.5.1.1 Oxygenation

Tissue oxygen delivery in sepsis may be complex and is affected by the interrelationship of multiple factors (Table 54.2). Optimal oxygen delivery globally or to specific organs is important (particularly in the setting of organ failure).

On the other hand, it is possible that high oxygen concentrations may be problematic, particularly if there are deficiencies in antioxidant defences (Salvemini and Cuzzocrea 2002) which may occur in several settings, including malnutrition.

Deleterious effects of high oxygen concentrations on the lung have been well documented for many years (Pagano and Barazzone-Argiroffo 2003). There is considerable animal evidence that high inspired oxygen concentrations in combination with mechanical ventilation may be related to increased pulmonary inflammation and lung damage (Sinclair et al. 2004; Altemeier and Sinclair 2007). Sinclair et al. also showed that in rabbit model ventilation with moderate tidal volumes using 50% oxygen (previously regarded as relatively safe) was associated with significant lung damage as compared to ventilation with room air (Sinclair et al. 2004). Experience in neonatology (Ehlert et al. 2006) has also highlighted the deleterious effects of high tidal volumes and hyperoxia.

Apart from effects on the lung, ventilation with high oxygen concentrations adversely affects alveolar macrophage and other immune functions (Baleeiro et al. 2003, 2006) and increases mortality from *Legionella pneumophila* (Tateda et al. 2003) in animal models.

Studies on the effect of hyperoxia on surgical site infections and outcomes following major surgery have yielded conflicting results (Pryor et al. 2004; Greif et al. 2000).

The effects of high oxygen concentrations on tissue in the setting of sepsis are controversial with studies reporting that high oxygen concentrations during resuscitation from haemorrhagic shock are associated with significant benefits (Brod et al. 2006), while other studies report opposite effects. These reports may be germane to patients with sepsis and multi-organ dysfunction which is associated with high oxidative stress (Alonso de Vega et al. 2000, 2002; Motoyama et al. 2003).

However, the findings are difficult to reconcile. In a model of porcine faecal peritonitis, ventilation with 100% oxygen (PEEP of 12–15 cm H₂O, tidal volumes of 8 ml/kg, long inspiratory

### Table 54.2 Tissues oxygen delivery problems in sepsis

| Blood oxygen content | Haemoglobin | Cardiac output | Organ perfusion | Tissue perfusion |
|----------------------|-------------|----------------|----------------|-----------------|
| **Concentration**    | Low in most shocked pediatric patients | Low in many situations | Low in many situations | Microvascular dysfunction |
| **Red cell function**| May be very common | May be very common | May be very common | Multiple components of microvascular dysfunction have been described in sepsis and may affect tissue oxygen delivery (Bateman et al. 2003) |

| Concentration often low (may be haemolysis as part of the syndrome); may be development of methaemoglobinemia in specific situations | May be abnormal as a result of sepsis; in conditions such as sickle cell disease may be exacerbation of abnormalities; transfused blood cells may have abnormal function (Sakr et al. 2007) | Hypoxaemia is very common in paediatric sepsis | Raised pressure within organs (kidney), spaces (intracranial, intrabdominal); may reduce perfusion | Multiple components of microvascular dysfunction have been described in sepsis and may affect tissue oxygen delivery (Bateman et al. 2003) |
times) was associated with improved splanchnic and renal blood flow together with improved organ function and reduced apoptosis in both the liver and lung when instituted either at the time of early peritonitis (Barth et al. 2008) or after established shock (Hauser et al. 2009).

Thus it would appear that in the early phases of resuscitation and ventilation for sepsis, the benefits of high inspired oxygen concentrations may outweigh its side effects. However once resuscitation is well underway, the benefits of high FiO₂ may be outweighed by increased lung damage and potentiation of inflammation throughout the body.

54.5.1.2 Carbon Dioxide
Permissive hypercarbia has been well recognized as a reasonable approach to lung protection in severe lung disease (Sevransky et al. 2004) and has been associated with improved outcomes in preterm neonates with respiratory failure (Mariani et al. 1999). In addition there is evidence that the acidosis related to hypercapnia may have lung protective effects (Laffey et al. 2000, 2004b).

More recently hypercarbic acidosis has been shown to have protective effects on the lung in experimental sepsis (Laffey et al. 2004a; Ni Chonghaile et al. 2008; Chonghaile et al. 2008) and also other organs (Costello et al. 2009).

Therefore, in respiratory failure due to sepsis, lung protective strategies such as permissive hypercapnia may need to be balanced against the possible deleterious effects due to pathology in other organs (e.g. the brain in meningitis) (Tasker and Peters 1998).

Although permissive hypercapnia has been accepted, there is little evidence published defining either upper levels of acceptable pCO₂ or limits of pH (Sevransky et al. 2004).

54.6 Optimization of Cardiovascular Function
Haemodynamic instability is a common feature of severe sepsis in children (Goldstein et al. 2005). While adults are likely to have low cardiac output with high systemic vascular resistance (Ceneviva et al. 1998; Carcillo et al. 2002). The impact of mechanical ventilation on haemodynamics depends on the interaction of many factors (Luecke and Pelosi 2005) including lung and chest wall mechanics (O’Quin et al. 1985) and characteristics of ventricular function (whether there is right, left or biventricular failure) (Bronicki and Anas 2009). Cardiopulmonary interactions are generally complex (Bronicki and Anas 2009), more so in the critically ill (Pinsky 1985, 1990, 1994, 1997, 2005, 2007; Jellinek et al. 2000), and may be affected by a wide variety of issues in sepsis.

Ventilation may alter venous return in patient with sepsis. For instance, in sepsis cardiac output may be decreased because of venodilatation and reduced venous return as well as high right atrial pressures due to positive pressure ventilation (Bronicki and Anas 2009). The relationship between ventilator pressures and right atrial pressure depends on the interaction between respiratory efforts and ventilator pressures, lung resistance and compliance, chest and abdominal wall compliance and the characteristics of the pericardium and cardiac muscle (Kingma et al. 1987). Generally lung compliance in children is relatively low, while chest wall compliance is high, with the result that ventilator pressures are poorly transmitted to the right atrium. This may however not be true in sepsis, where the chest wall may become very non-compliant as a result of oedema, inflammation and raised intra-abdominal pressure.

Ventilation may also affect both right and left ventricular outputs. Right ventricular output varies depending on pulmonary vascular tone and resistance which is highest at low and high lung volumes and lowest at functional residual capacity (Bronicki and Anas 2009; Jardin 1997; Jardin and Vieillard-Baron 2003). Thus positive pressure ventilation in sepsis may reduce pulmonary vascular resistance (and impedance) and improve right ventricular function by optimizing FiO₂, pH and lung volumes. However, over-distension of the alveoli may be associated with deterioration of right ventricular function.

Left ventricular afterload is also increased if negative intrathoracic pressures are generated.
during respiration (Bronicki and Anas 2009), and thus positive pressure ventilation may substantially reduce left ventricular afterload of patients in respiratory distress who have been generating very low intrathoracic pressures (as may be seen in sepsis). This may in turn improve cardiac output.

However, the left and right ventricles do not function in isolation and ventricular interactions that may determine the effect of ventilation on cardiac output (Tyberg et al. 2000; Biondi et al. 1988).

For instance, if respiratory distress and suboptimal cardiac output coexist, the respiratory muscles may consume a significant proportion of cardiac output. Mechanical ventilation may thus contribute significantly to an improvement in organ perfusion by reducing respiratory muscle activity (Aubier et al. 1981; Viires et al. 1983).

If left ventricular dysfunction is present in the septic patient, positive pressure ventilation may be associated with significant improvements in cardiac output (Bronicki and Anas 2009), while positive pressure ventilation may substantially reduce cardiac output if the patient is hypovolaemic.

In patients with acute lung injury recruitment, manoeuvres have been used in an attempt to improve respiratory function. These manoeuvres have been associated with significant decreases in cardiac output in both animal and human adult studies (Lim et al. 2004; Toth et al. 2007).

Cardiac function in severe sepsis can therefore be profoundly affected adversely or positively by positive pressure ventilation. The exact effects will depend on the specific situation and may have to be established by careful consideration of the physiological state and sometimes a process of trial and error.

54.7 Minimizing Damage to the Lungs

The optimal ventilatory pattern to minimize damage to the lungs will depend both on the disease and on the specific lung pathology.

Although the interplay is complex, the presence of predisposing factors (such as haemorrhagic shock) may exacerbate lung injury from inadequate ventilation (Bouadma et al. 2007), while inadequate ventilation may also exacerbate the inflammatory response to shock.

The presence of infection (or inflammation) also increases the lung and global inflammatory response to ventilation with high tidal volumes and low PEEP.

Nahum et al. (1997) demonstrated in a dog model that injurious patterns of ventilation (low PEEP and high tidal volume) significantly increased the translocation of bacteria from the lung into the circulation and the inflammatory responses within the lung.

Altemeier et al. showed in rabbits that ventilation with 10 ml/kg tidal volume had a synergistic effect, increasing lung injury, with the systemic administration of LPS (Altemeier et al. 2004). Bregeon et al. using a rabbit model showed that when E. coli lipopolysaccharide was administered intravenously, ventilation with zero PEEP and 10 ml/kg of tidal volume was associated with significant deterioration in lung mechanics, hypoxaemia and histological damage. Both authors demonstrated that mechanical ventilation alone did not induce lung injury, but mechanical ventilation together with aspiration of LPS was associated with an augmented inflammatory response and the development of ARDS changes (Altemeier et al. 2005).

Similar findings have been reported by others (Dhanireddy et al. 2006; O’Mahony et al. 2006; Bem et al. 2009) using a variety of models of ventilation during sepsis.

Thus a consistent theme in much experimental work in sepsis, mechanical ventilation (particularly with tidal volumes of 10 ml/kg or more) and high FiO$_2$ is associated with exacerbation of inflammatory responses both in the lung and throughout the body. There is little experimental data available on children, but it would seem reasonable to use “lung protective” strategies of ventilation in the setting of sepsis. There may also be a place for cautious use of “recruitment” followed by reduced pressure ventilation to minimize lung damage (Rimensberger et al. 1999).

Another consideration is the very common presence of fever in patients with sepsis. In an experimental study of ventilator-induced lung injury in rabbits, Suzuki et al. (2004)
demonstrated that lung damage using potentially injurious forms of ventilation was exacerbated by hyperthermia relative to hypothermia.

54.7.1 Acute Lung Injury (ALI) and Acute Respiratory Distress Syndrome (ARDS)

Severe sepsis is the most common cause of both ALI and ARDS in a population-based study of ALI and ARDS in the USA (Zimmerman et al. 2009). Pneumonia and sepsis were described as the main causes of ARDS in children in study from China (Yu et al. 2009).

ARDS/ALI has also been described in patients with malaria (less frequently in children) (Taylor et al. 2006; Mohan et al. 2008), dengue (Lum et al. 1995), Aspergillus (Anaissie 2008), tuberculosis and a whole host of viral infections.

Many studies have highlighted the potential benefits of ventilation with lower tidal volumes in adults with ARDS (Amato et al. 1995, 1998; The Acute Respiratory Distress Syndrome Network 2000; Meade et al. 2008; Brochard et al. 1998). Although there are fewer studies in the paediatric literature, the overwhelming weight of evidence is that paediatric mortality with ARDS has decreased substantially with lower tidal volume ventilation (Hanson and Flori 2006; Mehta and Arnold 2004; Albuali et al. 2007), higher PEEP levels and permissive hypercapnia. The importance of careful attention to ventilation is highlighted in a study of children in septic shock in which hand ventilation for greater than 6 h doubled mortality (Santhanam et al. 2008).

54.7.2 Respiratory Syncytial Virus Infection

The specific effect of various modes of ventilation depends on the underlying lung pathology (Naik et al. 1998). Greenough (2009) has recently reported a wide spectrum of lung disease in RSV infection ranging from obstructive lung disease with air trapping through restrictive lung disease with pneumonitis (Table 54.4). In response ventilatory support from CPAP through ECMO may be required in these children.

54.7.3 Tuberculosis

Tuberculosis may be responsible for a range of lung pathology in acute infection including ARDS (Agarwal et al. 2005a, b; Malhotra et al. 2005), expansile pneumonia (Goussard et al. 2004) and pneumonia (Goussard et al. 2008a), bronchopleural and broncho-oesophageal fistulae (Goussard et al. 2008b, 2007; Gie et al. 1998), laryngeal tuberculosis (du Plessis and Hussey 1987) and phrenic nerve damage related to mediastinal adenopathy (Goussard et al. 2009). Good outcomes can be achieved in children less than 6 months of age requiring ventilation for tuberculosis, but early diagnosis and therapy are essential (Goussard et al. 2008a).

A particular concern when ventilating children with tuberculosis is safety of staff and the need to identify family members with infectious tuberculosis as a potential source of nosocomial infection (Heyns et al. 2006; Schaaf et al. 2003).

54.7.4 Pertussis

Pertussis as a cause of severe pneumonia requiring intubation and ventilation has been underdiagnosed in some settings (Greenberg et al. 2007). The lung pathology in fatal cases reveals severe pulmonary hypertension and high white cell counts both of which may limit blood flow to the lung and poses significant challenges with ventilation (Table 54.3) (Paddock et al. 2008).

54.7.5 Pathologies with Limited Chest Wall Compliance

There are many potential reasons for reduction in chest wall compliance in patients with sepsis (Table 54.4). The decreased chest wall compliance may result increased pressures seen during
ventilation even with modest tidal volumes, but may also limit the chances of lung damage.

Complications in the pleural space such as pneumothorax and other air leaks seen with a number of organisms including *Pneumocystis jirovecii*, *Staphylococcus aureus* and *Streptococcus pneumoniae* (Sivit et al. 1995; Wong et al. 2000) may also decrease overall compliance and may pose challenges in ventilation.

Similarly, infections with organisms such as *Staphylococcus aureus* and *Streptococcus pneumoniae* have a higher incidence of empyema which may also decrease compliance of the chest (Li and Tancredi 2009; Soares et al. 2009; Langley et al. 2008). Effective drainage of fluid, air and pus collections is essential to effective ventilation and management of these children.

### Table 54.3 Ventilatory concerns related to sepsis and organ failure

| Area               | Description                                                                                                                                  | Possible Causes                                                                                     |
|--------------------|---------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| **Lungs**          | Changes in lung characteristics related to infective process in the lungs<br>Changes in lung characteristics related to generalized inflammatory process with leakage of fluid, cytokines and cells from the intravascular space<br>Pulmonary oedema related to fluid resuscitation and/or capillary leak syndromes<br>Interference with lung perfusion<br>Transfusion-related lung injury | Depending on the specific pathogen, there may be significant changes in airway resistance (bronchiolitis), in lung compliance (ARDS, pneumonia) Marked leucocyte invasion seen in pulmonary vasculature in pertussis (Paddock et al. 2008) |
| **Pleural space**  | Development of parapneumonic effusions and empyema<br>Development of pneumothoraces and bronchopleural fistulae |                                                                                                   |
| **Chest wall**     | Thickening and changes of chest wall characteristics related to the fluid shifts and inflammatory processes in sepsis<br>Changes in muscle function and particularly in diaphragmatic function related to the inflammatory processes |                                                                                                   |
| **Abdomen**        | Abdominal distension with raised intra-abdominal pressure<br>Organomegaly related to processes such as acute or even chronic hepatic failure |                                                                                                   |
| **Cardiovascular concerns** | Deterioration in cardiac muscle function related to inflammatory process<br>Development of large intrathoracic pressure changes related to acidosis and increased respiratory effort. This may significantly increase cardiac afterload<br>Fluid overload related to fluid resuscitation attempts |                                                                                                   |
| **Renal concerns** | Renal dysfunction is common in sepsis and may be associated with acidosis, electrolyte abnormalities and fluid overload. All of these may have adverse effects on the lungs |                                                                                                   |
| **Hepatic concerns** | Large liver (and ascites) may compromise diaphragmatic function<br>In the setting of chronic hepatic failure, there may be an increase in intrapulmonary shunting with associated hypoxaemia |                                                                                                   |
| **Musculoskeletal concerns** | Muscle weakness related to sepsis, organ failure or therapy |                                                                                                   |
Table 54.4 Pathology within the lung in the setting of sepsis

| Pathology                                      | Sepsis context                                                                 |
|-----------------------------------------------|-------------------------------------------------------------------------------|
| Normal lungs                                  | Patients with meningitis                                                      |
| Normal lung volumes with fluid extravasation into the lung | Pulmonary oedema related to fluid administration, renal failure with failure of fluid excretion, cardiac dysfunction with backward fluid pressure, leaky capillaries related to septic damage to the lung, etc. |
| Diffuse inflammation with low compliance and generalized atelectasis | ARDS                                                                          |
| Patchy changes with areas of hyperinflation and areas of collapse | Bronchopneumonia                                                              |
| Diffuse inflammation with air trapping         | Bronchiolitis                                                                  |
| Coagulopathy-related problems with areas of diffuse haemorrhage | ARDS                                                                          |
| Transfusion-related lung injury                |                                                                               |

54.8 Infection Control Issues

Mechanical ventilation of infected patients poses a risk to staff and other patients. Effective antibiotic therapy will usually render bacterial pathogens noninfective rapidly, but there are considerable concerns with viral pathogens and organisms such as tuberculosis.

Ventilator care of infected patients may be associated with nosocomial spread of infection via a variety of methods including aerosolization of organisms and contamination of ventilators, and considerable care must be implemented to prevent this risk.

Staff caring for patients with respiratory disease are also at risk of infection, particularly during procedures such as intubation or endotracheal suctioning. The experience from epidemics such as SARS suggests that health-care workers in the intensive care environment need substantial training in the use of self-protective strategies (Chia et al. 2005), while organizations need to consider the processes for staff protection (Moore et al. 2005), and ongoing research is required to assess the risk related to aerosolization of organisms and related issues (Yassi et al. 2005).

A particular concern is patients with immune deficiencies who may continue to shed pathogens a long time after the initial presentation (Arbiza et al. 2006).

54.9 Airway Humidification and Clearance in Sepsis

It is generally accepted that sputum characteristics are altered in patients with infection. Children are particularly at risk of airway obstruction from secretions as a result of the relatively small endotracheal airway utilized during endotracheal intubation and ventilation. Particular attention needs to be paid to the issues of adequate airway humidification during ventilation although the literature on this topic is extremely limited (Branson 2007; Niel-Weise et al. 2007; Ricard et al. 2006).

Suctioning is required to maintain patency of endotracheal tubes but may be associated with many and varied adverse effects (Morrow and Argent 2008). The recommendations for suctioning were recently reviewed (Morrow and Argent 2008) and include the following: no routine suctioning (except perhaps in patients on neuromuscular blockade), use appropriate size suction catheters (2X the internal diameter of the endotracheal tube (mm) will give the approximate size (FG) of the suction catheter to be used), use the minimum suction pressure required to remove secretions (with a maximum of 360 mmHg), do not use saline routinely, and limit the duration of any particular suctioning manoeuvre.

Conclusions

Sepsis in children is associated with a wide range of clinical syndromes and challenges. Appropriate ventilation in patients with sepsis requires a broad understanding of the effects of ventilation on the cardiovascular and respiratory systems, as well as local and global inflammatory responses.

In addition, it is extremely important to ensure that nosocomial spread of infection is limited and that staff are protected from the possibility of acquiring infections from their patients.
Essentials to Remember

- Sepsis may be associated with a wide variety of problems in multiple organs.
- Aims of ventilatory support will be related to the particular organs that are affected by sepsis.
- Ventilatory support must be focused on providing appropriate blood gases for the particular patient context while causing the least possible damage to the lungs.
- The effects of ventilatory support on the cardiovascular system are closely related to the specific pathophysiology in a particular patient. Cardiovascular responses to ventilation must be carefully monitored with appropriate adjustment of ventilation.
- Infection control measures, to protect both the ventilated patient and the staff and other patients, are an essential component of ventilatory support.
- Patients with sepsis may need special attention to the adequate clearance of secretions on ventilation, but this must be done with great care.

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