Chapter 13
Acute Respiratory Failure

John Victor Peter

Key Points

- Respiratory failure may be categorised as hypoxaemic and hypercapnic respiratory failure.
- Simple algorithms help to diagnose and understand the causes of respiratory failure.
- Management goals include treating the underlying problem, improving oxygenation and/or carbon dioxide levels and limiting the deleterious effects of such treatment.
- Respiratory support can be provided by non-invasive devices or by invasive ventilation.

Introduction

Respiratory failure represents the failure of the lung to maintain adequate gas exchange and is characterised by abnormalities of arterial blood gas tensions. Traditionally it is defined using a PaO_2 cut-off of <8 kPa [60 mmHg] with or without hypercarbia [$PaCO_2$ >6 kPa (46 mmHg)]. The onset of respiratory failure is usually acute or subacute. In some patients, such as in chronic obstructive pulmonary disease (COPD), the respiratory failure may be long-standing and chronic. Although sometimes, this demarcation may not be distinct, the management of respiratory failure is often dependent on the extent and duration of symptoms.

J.V. Peter, MD, DNB, MAMS, FRACP, FCICM, FICCM
Medical Intensive Care Unit, Christian Medical College, Vellore 632 004, India
e-mail: peterjohnvictor@yahoo.com.au

S.S. David (ed.), *Clinical Pathways in Emergency Medicine: Volume I*,
DOI 10.1007/978-81-322-2710-6_13

Physiology

The respiratory apparatus involves three components – the *pacemaker*, the *pump with tubes* and the *gas exchanger*. Abnormalities of any of these three components can result in respiratory failure. The central nervous system (CNS) functions as the *pacemaker*, setting the pace (respiratory rate) and the amplitude (tidal volume). This net ventilatory drive determines minute ventilation, which is the product of tidal volume and rate. An increased respiratory drive thus results in hyperventilation, while reduced respiratory drive results in hypoventilation. The *pump with the tubes* may be considered akin to bellows, comprising of the lungs and airway, and serves as a device that enables the delivery of adequate alveolar ventilation. Two factors influence the efficiency of the pump – resistance and compliance. Increased resistance of the airway or reduced compliance of the lung or the chest wall reduce the efficiency of the pump and increase the work of breathing (WOB). A sustained increase in the WOB may result in ventilatory fatigue, hypoventilation and respiratory failure. The third component of the respiratory apparatus, the *gas exchanger* comprises of bags of air (alveoli) surrounded by pulmonary capillaries. The pump delivers gas to the alveoli, wherein gas transfer occurs passively across a pressure gradient. Two factors determine the efficiency of this gas transfer – the alveolar-capillary interface and the transit time of blood in the pulmonary capillaries. The transit time of blood in the pulmonary capillaries of about 0.7 s is sufficient for gas exchange unless there are problems with the alveolar-capillary interface. Conditions that increase the thickness of the alveolar-capillary interface (e.g. fluid in the alveoli, interstitial inflammation) impair gas transfer. However, since the diffusion capacity of CO_2 is about 20 times that of O_2, such abnormalities of the gas exchanger generally result in pure hypoxaemia unless the extent of alveolar involvement is marked or if respiratory fatigue ensues due to increased WOB.

Classification

Respiratory failure may be classified based on the blood gas abnormality (*physiologic approach*) or on the pathophysiologic process (*pathophysiologic approach*) that causes respiratory failure. Using a physiologic approach, type I respiratory failure or *hypoxaemic respiratory failure* is defined as hypoxaemia (PaO_2 <60 mmHg) with normal or low $PaCO_2$, while type II respiratory failure *or hypercapnic respiratory failure* is defined as the presence of hypercarbia ($PaCO_2$ >46 mmHg) with or without coexistent hypoxaemia. Using the pathophysiologic approach, respiratory failure is classified into four types. In type I respiratory failure, the pathophysiologic abnormality is *alveolar flooding* resulting in intra-pulmonary shunting. These patients have a predominant hypoxaemic respiratory failure, although in very severe cases, CO_2 retention may supervene. Common aetiologies include cardiogenic and non-cardiogenic pulmonary oedema, pneumonia and alveolar haemorrhage

(Table 13.1). Type II respiratory failure is due to *alveolar hypoventilation*. In this type of respiratory failure, the pathophysiologic abnormality is hypoventilation either due to a process in the central nervous system (cortical, subcortical, brainstem or spinal cord), peripheral nerves, muscle, neuromuscular junction or the alveoli (alveolar hypoventilation). These patients typically manifest hypercapnic respiratory failure with or without hypoxaemia. Type III respiratory failure occurs due to *lung atelectasis*. Since this is common in the post-operative setting, it is also termed *perioperative respiratory failure*. Patients manifest hypoxaemic respiratory failure. Type IV respiratory failure occurs due to *hypoperfusion of respiratory muscles* as in circulatory shock. In normal individuals <5 % of the cardiac output is utilised for the work of breathing. In patients with shock, due to increased work of breathing,

Table 13.1 Classification of respiratory failure and causes

Pathophysiologic type of respiratory failure	Physiologic type of respiratory failure	Causes
Type I respiratory failure – alveolar flooding	Hypoxaemic respiratory failure[a]	Fluid – alveolar and interstitial oedema (cardiac and non-cardiogenic pulmonary oedema, ARDS)
		Pus/infection – alveolar and interstitial infection (pneumonia, interstitial pneumonitis)
		Blood – alveolar haemorrhage
		Protein – alveolar proteinosis (rare)
Type II respiratory failure – alveolar hypoventilation	Hypercapnic respiratory failure	CNS depression – drug overdose and poisoning, infection, trauma, stroke
		Spinal cord – poliomyelitis, transection, myelitis
		Peripheral nerves – Guillain-Barre syndrome, phrenic nerve injury, amyotrophic lateral sclerosis
		Chest wall – kyphoscoliosis, chest wall injuries, ankylosing spondylitis
		Muscle – myasthenia gravis, myopathies, hypokalaemia, hypophosphataemia, polymyositis
		Alveolar hypoventilation – COPD, severe cystic fibrosis, end-stage pulmonary fibrosis, airway obstruction
Type III respiratory failure – lung atelectasis	Hypoxaemic respiratory failure	Post-operative atelectasis (intra-pulmonary shunting), basal atelectasis due to intra-abdominal pathology, pulmonary embolism[b]
Type IV respiratory failure – hypoperfusion of respiratory muscles	Hypercapnic respiratory failure	Cardiogenic shock, hypovolaemic shock, septic shock

[a]Hypoxaemic respiratory failure also occurs in high altitude due to a low inspired oxygen concentration
[b]Ventilation/perfusion mismatch is also an important contributor of hypoxaemia in patients with pulmonary embolism

up to 40 % of the cardiac output may be utilised for breathing. These patients manifest hypercapnic respiratory failure due to ventilatory fatigue.

Approach to Hypoxaemic Respiratory Failure

The pathophysiologic mechanisms that may contribute or result in hypoxaemia are (a) low inspired oxygen, (b) ventilation/perfusion (*V*/*Q*) mismatch, (c) shunt, (d) hypoventilation, (e) diffusion abnormality and (f) reduced mixed venous oxygen. In the clinical setting, the common pathophysiologic abnormalities that cause hypoxaemia include *V*/*Q* mismatch, shunting and hypoventilation. More than one pathophysiologic process may coexist in the same patient. Pure diffusion abnormalities are uncommon. A marked reduction in the oxygen content of the blood returning to the lungs (mixed venous oxygen), as occurs with reduced oxygen delivery or increased tissue consumption, may also result in the need for more oxygen to be transported from the inspired gas to the blood to normalise the PaO_2. If the lungs are normal, this does not have a significant effect. However, in the presence of a *V*/*Q* abnormality or a shunt, the effect is magnified as the shunted blood has a lower than normal oxygen content.

The alveolar-arterial oxygen difference ($PAO_2 - PaO_2$) and response to oxygen therapy help in ascertaining the cause of hypoxaemic respiratory failure (Fig. 13.1). The alveolar-arterial (A-a) oxygen gradient (difference) is calculated using the formula given below. It must be noted that the term 'alveolar gradient', although commonly used, is a misnomer since what is calculated is the gap between the alveolar and arterial O_2 and not a true gradient in PaO_2 from the alveolar space to the blood.

$$\text{A-a difference} = \left[FiO_2 \left(P_{atm} - P_{H_2O} \right) - PaCO_2 / 0.8 \right] - PaO_2$$

FiO_2, fixed inspired oxygen concentration; P_{atm}, atmospheric pressure; P_{H2O}, partial pressure of water at body temperature; $PaCO_2$, partial pressure of carbon dioxide; and PaO_2, partial pressure of oxygen in the arterial blood: Normal A-a difference is 5–15 mmHg. The formula [Age (in years)/4] + 4 may be used to calculate the A-a difference adjusted for age.

An increased A-a difference is the result of abnormalities of gas exchange within the lung (intra-pulmonary processes). Thus, intra-pulmonary processes such as *V*/*Q* mismatch, shunt and diffusion abnormalities would increase the A-a difference. The extent of increase is usually more pronounced with pure pulmonary processes than with mixed pulmonary and extra-pulmonary processes.

In the evaluation of a hypoxaemic patient, the first step is to ascertain the CO_2 level. A high CO_2 (>46 mmHg), in the absence of metabolic alkalosis as the cause for a compensatory increase in CO_2, suggests hypoventilation. In such patients, the A-a difference helps differentiate pure hypoventilation from a mixed process (Fig. 13.1). In the absence of hypercarbia, an increase in the A-a difference suggests either an increase in the A-a difference suggests either a shunt, *V*/*Q* mismatch or diffusion abnormality. Hypoxaemia due to low inspired oxygen concentration does not increase

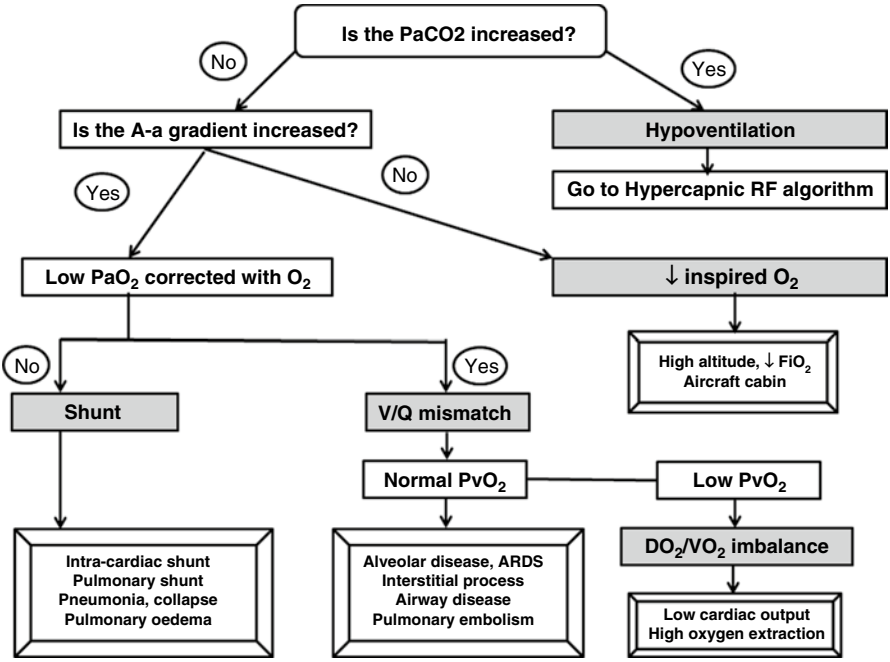

Fig. 13.1 Approach to hypoxaemic respiratory failure. The alveolar-arterial (A-a) oxygen difference ($PAO_2 - PaO_2$) and response to oxygen therapy help in the assessment of the cause of hypoxaemic respiratory failure (RF) as shown in the diagram. *V/Q* ventilation/perfusion, PaO_2 arterial partial pressure of oxygen, PvO_2 venous partial pressure of oxygen, DO_2/VO_2 oxygen supply/oxygen utilisation ratio

A-a difference and responds to supplemental oxygen therapy. In the setting of a high A-a gradient, improvement in oxygenation with supplemental oxygen would suggest *V/Q* mismatch, while lack of improvement would suggest a shunt (Fig. 13.1).

Aetiology of Acute Hypoxaemic Respiratory Failure

The aetiology of acute hypoxaemic respiratory failure can be broadly classified as:

(a) Parenchymal pathology

1. Increased capillary pressure: cardiogenic pulmonary oedema and fluid overload
2. Increased capillary permeability: acute respiratory distress syndrome (ARDS) due to pulmonary and extra-pulmonary causes
3. Inflammatory: infection (lobar and bronchopneumonia, interstitial pneumonitis), alveolitis (acute interstitial pneumonitis, acute vasculitis), and haemorrhage (alveolar)
4. Atelectasis

(b) Pleural: pneumothorax and pleural effusion
(c) Airway related: acute severe asthma
(d) Vascular: pulmonary embolism and circulatory shock

Management of Acute Hypoxaemic Respiratory Failure

The principles of management of acute hypoxaemic respiratory failure include (a) treatment of the underlying cause (specific treatment), (b) improving oxygen delivery to the tissues, (c) limiting potentially damaging therapies and (d) reducing tissue oxygen demand.

Specific therapy involves the treatment of the cause that precipitated respiratory failure. Examples of this would include antibiotic therapy for sepsis, bronchodilators for acute asthma, thrombolysis for pulmonary embolism, paracentesis for pleural effusion or diuretic and vasodilator therapy for heart failure.

Oxygen delivery to the tissues can be increased by improving oxygenation, maintaining haemoglobin and by optimising cardiac output. Oxygenation can be improved by increasing the FiO_2 (up to 1.0) or by adding positive end-expiratory pressure (PEEP). PEEP can be provided by non-invasive ventilation or through invasive mechanical ventilation. Tissue oxygen demand can be reduced by control of fever, sepsis or seizures. Increased WOB can also increase oxygen demand significantly, and in certain situations, particularly in patients with shock, it may be prudent to intubate and ventilate these patients. Potentially damaging therapy should be limited by minimising the use of high oxygen concentration for protracted periods and by adopting lung protective ventilatory strategies.

Oxygen Delivery Devices

Oxygen delivery devices should be able to deliver controlled and consistent oxygen concentrations. Oxygen delivery devices are classified based on flow (low flow or high flow), performance (variable or fixed) and whether they are non-rebreathing or rebreathing systems (Table 13.2). Rebreathing systems allow some mixture of exhaled gases, while non-rebreathing systems have one-way valves. Closed mask systems connected to non-breathing devices ensure the delivery of set volumes (e.g. continuous positive airway pressure (CPAP) devices).

Low flow devices are so called as they deliver oxygen at less than the peak inspiratory flow rate (PIFR). Examples include nasal cannula, simple face mask and partial rebreather masks. High-flow devices deliver oxygen at flow rates higher than the PIFR. These systems have adequate reservoir capacity that enables the delivery of adequate flow. Examples include venturi devices, T-piece or breathing circuits (e.g. CPAP circuits) with reservoir bags or connected to high-flow oxygen source.

Table 13.2 Oxygen delivery devices

Categorisation based on flow	Example	Performance	Oxygen flow rate (per min)	FiO_2 delivered
Low-flow device	Nasal cannula	Variable	2–4 l[a]	24–35 %
	Simple face mask	Variable	5–10 l	40–60 %
	Tracheal mask	Variable	5–10 l	40–60 %
	Partial rebreathing mask with reservoir bag	Variable	4–10 l	35–60 %
High-flow device	Venturi	Fixed	3–15 l	24–60 %
	High-flow warmed nasal devices	Fixed using blenders	10–40 l	40–100 %
	Non-rebreather mask with reservoir bag	Variable	8–10 l	60–90 %

[a]Higher flow rates are uncomfortable

Table 13.3 Example of a variable performance device

Parameter	Patient 1	Patient 2
Tidal volume	400 ml	400 ml
Respiratory rate	10	20
Minute ventilation	4000 ml	8000 ml
I:E ratio	1: 2	1: 2
Inspiratory time	2 s	1 s
Oxygen through cannula	2 l/min (2000 ml)	2 l/min (2000 ml)
Additional air mix	2000 ml	6000 ml
Ratio of oxygen: air mix	1: 1	1: 3

In a variable performance device, the oxygen concentration of the air-oxygen mix reaching the alveoli is not constant; the final O_2 concentration is dependent on the oxygen flow rate, size of the reservoir and the respiratory rate of the patient. For a fixed tidal volume, when the respiratory rate increases, since the amount of oxygen given through the device (e.g. nasal cannula) is fixed (e.g. 2 l), the resultant air-oxygen mixture at the higher respiratory rate contains less oxygen than when the rate is lower (see example in Table 13.3). A fixed performance device on the other hand is not influenced by these factors and is able to provide a fixed inspired oxygen concentration irrespective of the patient's respiratory rate (e.g. a venturi device).

The choice of the device is based on the severity of hypoxaemia and whether a fixed performance device is essential. In patients with mild hypoxaemia (PaO_2 60–70 mmHg on room air), a nasal cannula or a simple mask may be sufficient. Nasal cannula is well tolerated and patients are able to eat and drink while on this device. However, delivery of oxygen through a nasal device can be associated with drying of the nasal mucosa. With moderate hypoxaemia (PaO_2 50–60 mmHg), a partial rebreather mask or venturi device may be used; the latter is preferred for COPD patients. In patients with severe hypoxaemia (PaO_2 <50 mmHg) and those not respond-

ing to simpler devices, non-rebreather systems (e.g. CPAP, non-invasive ventilation, Ambu bag, Bains) or invasive mechanical ventilation may be considered.

Intubation and mechanical ventilation are sometimes required for patients with severe or persistent hypoxaemic respiratory failure. Ventilatory support offloads the respiratory muscles, reduces the WOB and reduces oxygen demand. In addition, ventilation (invasively or non-invasively) allows the application of PEEP. Several studies have demonstrated the beneficial effect of PEEP. PEEP helps by improving oxygenation (by increasing functional residual capacity and increasing alveolar volumes), improving lung compliance (by preventing alveolar de-recruitment and reducing pulmonary venous congestion in heart failure patients), reducing dead space (keeping the alveoli open), improving cardiovascular function (by reducing afterload) and reducing the work of breathing. The usual PEEP level in the intensive care unit (ICU) is 5–15 cm H_2O; higher levels have been used in severe ARDS.

Newer methods of oxygen delivery in severe ARDS with refractory hypoxaemia have been with the use of extracorporeal membrane oxygenators (ECMO).

Approach to Hypercapnic Respiratory Failure

Hypercapnia results either from increased CO_2 production or reduced CO_2 elimination or a combination of both. Increased CO_2 production (Fig. 13.2) may occur with increased muscle activity (spasms, convulsions), hypermetabolic states (fever, sepsis) and carbohydrate-rich feeds. In this setting, hypercapnia occurs if CO_2 elimination does not keep pace with CO_2 production. Reduced CO_2 elimination occurs due to reduced pacemaker function, impaired respiratory pump function, airway problems and abnormalities of the gas exchanger. Generally, pure abnormalities of the pulmonary parenchyma result in low *V*/*Q* units with hypoxaemia without hypercapnia. However, when *V*/*Q* abnormalities are very severe or when there is coexistent respiratory muscle fatigue, hypercapnia may ensue. Hypercapnia may also occur when breathing a gas containing CO_2. This may occur due to rebreathing exhaled gases as a result of improper ventilatory expiratory connections (tube or expiratory port).

Hypercapnia may be approached as pulmonary or extra-pulmonary causes or a combination of both. Extra-pulmonary causes include CNS and peripheral nervous system (PNS) disorders, respiratory muscle dysfunction (due to a primary muscle disease or neuromuscular dysfunction) or due to chest wall abnormalities (Table 13.1). Pulmonary causes include airway obstruction (foreign body, epiglottitis, obstructive sleep apnoea), severe COPD and end-stage lung disease due to other parenchymal processes. An increase in the A-a difference would suggest a coexisting *V*/*Q* abnormality or a shunt (Fig. 13.2). In the absence of an increased A-a gradient, assessment of maximal inspiratory pressure (MIP or PI max) and/or maximal expiratory pressure (MEP or PE max) would help diagnose respiratory muscle weakness. MIP primarily reflects the strength of the diaphragm and other inspiratory muscles, while MEP reflects the strength of the abdominal muscles and other expiratory muscles. The

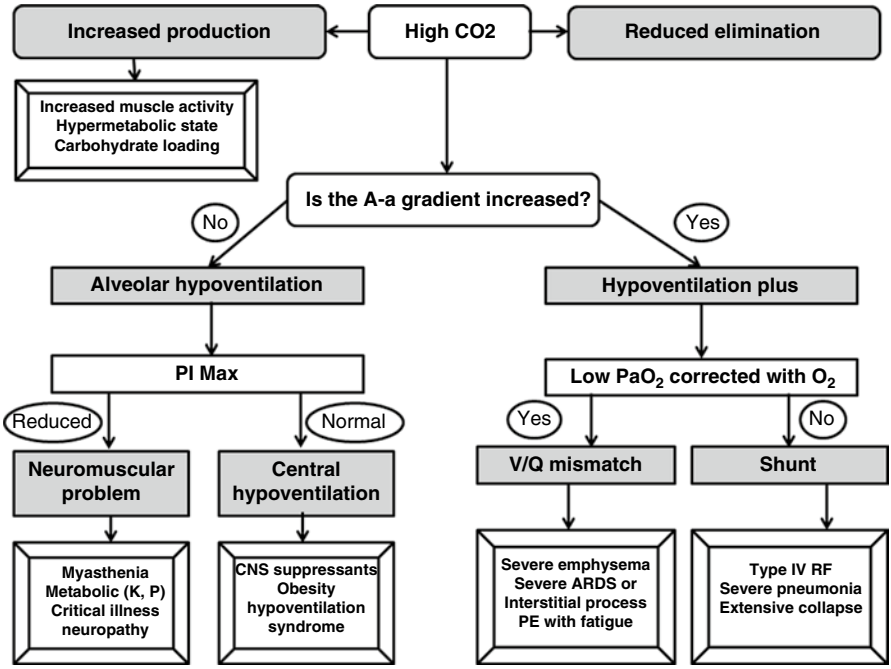

Fig. 13.2 Approach to hypercapnic respiratory failure. Hypercapnic respiratory failure may be due to increased CO_2 production or reduced CO_2 elimination of a combination of both. The alveolar-arterial (A-a) oxygen difference ($PAO_2 - PaO_2$) helps to ascertain if alveolar hypoventilation is occurring independently or in conjunction with a *V/Q* (ventilation/perfusion) mismatch or shunt. *PI max* maximal inspiratory pressure

sniff nasal inspiratory pressure (SNIP), an easy-to-use first-line tool, may be used as an alternative diagnostic test for respiratory muscle weakness. If these tests suggest respiratory muscle weakness, further evaluation is warranted to ascertain the cause. These include primary muscle diseases (myopathies, polymyositis), neuromuscular transmission defect (myasthenia gravis), metabolic disorders (hypokalaemia, hypophosphataemia) and critical illness polymyoneuropathy. Normal respiratory muscle function would suggest a central cause for hypercapnia. This includes obesity-hypoventilation syndrome and respiratory centre depression due to overdose, CNS infection, trauma, tumour or stroke (Table 13.1).

The $PaCO_2$ must always be considered in relation to the pH. This is particularly helpful in distinguishing acute and chronic hypercapnic respiratory failure as well as stable chronic hypercapnic respiratory failure and acute-on-chronic hypercapnic respiratory failure. In acute hypercapnic respiratory failure, there is always a shift in the pH, since compensatory mechanisms take time, unless the respiratory failure is mild. However, in chronic hypercapnic respiratory failure, since metabolic compensation occurs, the pH is usually close to normal, often >7.32 and sometimes even normal. Thus, the distinction between chronic respiratory failure and acute-on-chronic respiratory failure is not made on the CO_2 level but on the pH, where any

acute process superimposed on a chronic stable state would shift the pH. Thus, a drop in pH to <7.30 in such patients would be diagnostic of acute CO_2 retention.

Aetiology of Hypercapnic Respiratory Failure

The aetiology of acute hypoxaemic respiratory failure can be broadly classified as:

(a) Central nervous system pathology:

1. Cortical: stroke, infection, trauma, drug overdose and acute disseminated encephalomyelitis
2. Brainstem depression: stroke, basal meningitis, trauma and obesity-hypoventilation syndrome
3. Spinal cord: trauma, infectious and post-vaccine myelitis and poliomyelitis

(b) Peripheral nervous system pathology: Guillain-Barre syndrome, phrenic nerve injury, amyotrophic lateral sclerosis and critical illness polyneuropathy
(c) Neuromuscular: myasthenia gravis
(d) Muscle: critical illness myopathy, metabolic (hypokalaemia, hypophosphataemia, magnesium depletion) and polymyositis
(e) Chest wall: flail chest, kyphoscoliosis and ankylosing spondylitis
(f) Alveolar hypoventilation due to pulmonary causes: COPD, severe cystic fibrosis, end-stage pulmonary fibrosis and airway obstruction

Management of Acute Hypercapnic Respiratory Failure

As with acute hypoxaemic respiratory failure, the goals of treatment of acute hypercapnic respiratory failure include (a) treatment of the underlying cause (specific treatment), (b) reducing CO_2 production, (c) improving CO_2 elimination and (d) limiting potentially damaging therapies.

Specific therapy involves treating the precipitating cause. This would include antibiotics to treat infection, bronchodilators and steroids for exacerbation of COPD or the reversal of the central or peripheral nervous system problem that resulted in hypercapnic respiratory failure. CO_2 production may be reduced by controlling fever and excess motor activity (convulsions) and by reducing carbohydrate intake. Since the respiratory quotient for carbohydrate is 1.0 and for fat is 0.7, this is particularly important in the setting of COPD exacerbation with difficulty in weaning where reduction in the carbohydrate intake may translate to easier weaning.

CO_2 elimination can be enhanced by increasing the respiratory drive and by improving lung mechanics. Respiratory drive can be increased by reducing or minimising the use of sedation and by using drugs that increase respiratory drive, particularly in the context of COPD. Although the benefit has not been proven in

randomised trials, drugs such as acetazolamide, medroxyprogesterone acetate and other centrally acting CNS stimulants have been used in COPD exacerbations. Lung mechanics can be improved by manoeuvres such as propping up the patient, use of analgesics to reduce chest pain as in chest wall injuries, reducing airway resistance (use of bronchodilators and bronchial hygiene), improving lung compliance (by reducing abdominal distension or pleurocentesis), improving respiratory muscle performance (by ensuring adequate oxygenation, tissue perfusion) and correcting electrolyte abnormalities (such as hypokalaemia, hypophosphataemia). Drugs such as xanthines (theophylline) which improve diaphragmatic contractility may be considered. However, given the narrow therapeutic window and toxicity profile, its use is limited.

Ventilatory support, either using non-invasive ventilation or invasive ventilation, may be required in patients with respiratory fatigue and persistent hypercapnic respiratory failure. Ventilatory support offloads the respiratory muscles, reduces the work of breathing and rests the muscles. Since CO_2 elimination is dependent on minute ventilation, appropriate targets should be set for tidal volume and respiratory rate in order to achieve minute ventilation that would correct the physiologic abnormality while the underlying problem is dealt with. Care should be taken during ventilation to limit lung injury due to high pressures (barotrauma) or high volume (volutrauma) and use of an appropriate level of PEEP to reduce atelectrauma. In patients where conventional ventilatory strategies are not sufficient to ensure CO_2 elimination and improvement in pH, extracorporeal CO_2 removal devices can be considered.

Conclusions

A systematic approach to respiratory failure is important in ascertaining the cause of respiratory failure. Since the respiratory treatment of the two physiologic types of respiratory failure is different, knowledge of the mechanisms of respiratory failure and the basis of supportive treatment is crucial. All such respiratory treatment and support would only be beneficial if the underlying disease process that resulted in respiratory failure is adequately and appropriately managed.

Further Reading

1. ATS – Oxygen delivery methods. http://www.thoracic.org/clinical/copd-guidelines/for-health-professionals/exacerbation/inpatient-oxygen-therapy/oxygen-delivery-methods.php. Accessed Aug 2014.
2. British Thoracic Society Standards of Care Committee. Non-invasive ventilation in acute respiratory failure. Thorax. 2002;57:192–211.
3. Fitting JW. Sniff nasal inspiratory pressure: simple or too simple? Eur Resp J. 2006;27: 881–3.

4. Gunning KEJ. Pathophysiology of respiratory failure and indications for respiratory support. Surgery (Oxford). 2003;21:72–6.
5. Irwin RS, Cerra FB, Rippe JM. Irwin and Rippe's intensive care medicine. Sheffield, UK: Lippincott Williams & Wilkins; 1999.
6. John G, Peter JV, Subramani K, Pichamuthu K, Chacko B. Essentials of critical care, vol. I, 8th ed. Division of Critical Care, Christian Medical College, Vellore; 2011.
7. Longo DL, Kasper DL, Jameson JL, Fauci AS, Hauser SL, Loscalzo JL. Harrison's principles of internal medicine. 18th ed. TX, USA: Mc-Graw Hill Medical; 2011.
8. Roussos C, Koutsoukou A. Respiratory failure. Eur Resp J. 2002;22 Suppl 47:3a–14.
9. Ward JJ. High-flow oxygen administration by nasal cannula for adult and perinatal patients. Respir Care. 2013;58:98–122.