Part II: Respiratory Failure

Chapter 18: Oxygen Therapy

T. E. Oh

Oxygen is required in aerobic metabolic pathways to produce biological energy from food fuels. With inadequate oxygenation, anaerobic metabolism leads to decreased biological energy and harmful lactic and metabolic acidosis. Oxygen therapy is thus indicated whenever tissue oxygenation is impaired, in order to allow essential metabolic reactions to occur, and to prevent complications attributed to hypoxaemia.

The common clinical indications are:

1. Acute respiratory failure:

(a) without CO_2 retention, i.e. asthma, pneumonia, pulmonary oedema, and pulmonary embolism;

(b) with CO_2 retention, i.e. chronic bronchitis, chest injuries, unconscious drug overdose, postoperative hypoxaemia, and neuromuscular disease.

2. Acute myocardial infarction.

3. Cardiac failure.

4. Shock of any cause.

5. Increased metabolic demands, i.e. burns, multiple injuries, and severe infections.

6. Postoperative states.

7. Carbon monoxide poisoning.

Arterial Oxygen Tension (PaO_2)

Tissue oxygenation depends upon oxygen delivery and PaO_2. It is difficult to suggest a "safe" PaO_2 value at which hypoxia poses few significant problems. Each situation needs to be judged by the requirements for oxygen and the availability of oxygen. In general, additional inspired oxygen is required when PaO_2 is 60 mmHg (8.0 kPa) or less, and profound hypoxaemia is present and death is imminent, when PaO_2 is less than 30 mmHg (4.0 kPa). The clinical significance of some common PaO_2 and saturation values are listed (Table 1).

Oxygen Dissociation Curve

Tissue oxygenation depends partly on the Hb oxygen saturation and the shift of the oxygen dissociation curve. A shift of the curve to the right (Fig 1) favours Hb unloading of oxygen, and thus oxygen delivery to the tissues. Conversely, a shift to the left increases the

affinity of Hb for oxygen with reduced tissue oxygenation. The factors influencing the position of the curve are shown in Table 2.

Oxygen Flux and Requirements

Oxygen delivery to the cells is represented by the oxygen cascade (Table 3). The supply of oxygen is dependent upon the haemoglobin (Hb), oxygen saturation % (SaO_2) and cardiac output (Q). "Oxygen flux" denotes the total amount of oxygen delivered to the body per minute and is given by the equation:

Oxygen flux = 1.34 x Hb in g/dL x (SaO_2/100) x (Q in mL/min)/100 = 1000 mL/min

(1.34 = oxygen-carrying capacity of Hb in mL/g Hb.) The amount of oxygen carried dissolved in blood is negligible.

Hence the oxygen supply for a normal adult is approximately 1000 mL/min. However, not all of this amount is available for cellular utilization. Oxygen diffuses from tissue capillaries to mitochondria in cells. Mean tissue PO_2 varies from organ to organ and is higher near capillaries, especially near the arteriole end. Although mitochondria in tissue cells may operate at a PaO_2 of 8-40 mmHg (1.06-5.32 kPa), diffusion requires a capillary-tissue cell gradient. Thus tissue extraction of oxygen from blood is generally limited, and mitochondrial function jeopardized, at a PaO_2 of less than 300 mmHg (4.0 kPa) or a saturation of 30%. The available oxygen/min is therefore less than the supply (by about 250-300 mL/min) and is approximately 700 mL in a normal man.

Normal oxygen consumption at rest is about 200-250 mL/min. The oxygen reserve (availability minus consumption) in a normal man at rest is thus about 450-500 mL/min. Some factors in the sick person increase oxygen consumption greatly, i.e. fever, sepsis, shivering, restlessness and hypercatabolism. When other associated factors concomitantly reduce oxygen supply and availability, then the oxygen reserve may be reduced to critical levels and place the patient in jeopardy. A concept of minimum or "critical" oxygen flux of 400 mL/min is useful, below which tissue hypoxia may occur. Thus the use of additional oxygen to relieve hypoxaemia must be considered with measures to:

1. Reduce oxygen requirements (i.e. by cooling, paralysis, and controlled ventilation).

2. Increase oxygen availability (by correcting anaemia, low cardiac output, and adverse factors which shift the dissociation curve to the left).

Methods of Oxygen Therapy

The basic requirements of methods or devices for use in oxygen therapy are:

1. Control of fractional inspired oxygen concentration (FIO_2).
2. Prevention of excessive CO_2 accumulation.
3. Minimal resistance to breathing.
4. Efficient and economical use of oxygen.
5. Acceptance by patients.

The methods available to raise PaO_2 are shown (Table 4) and classified below. Oxygen head hoods, tents and incubators are used in paediatrics but are impractical in adults. Anaesthetic circuits and resuscitator bags are used to preoxygenate patients prior to endotracheal intubation. Oxygen administration is thus achieved largely by facemasks or nasal catheters.

Classification of Apparatus and Devices

It is important to know if the FIO_2 delivered by the apparatus will vary with the patient's ventilation. Apart low-flow spontaneous breathing circuits, some manual resuscitator bags, and ventilators, no device will deliver 100% oxygen, unless the oxygen is supplied at a rate greater than peak inspiratory flow rate (PIFR). PIFR in adults is about 25-35 L/min at rest, increasing markedly to over 60 L/min in dyspnoeic states. The apparatus and devices for oxygen therapy are classified below.

A. Fixed Performance Systems (FIO_2 is independent of patient factors.)

1. *High-flow Venturi-type Masks*

Oxygen flow entrains air by the venturi principle to delivery a fixed FIO_2 which remains accurate. Ventimasks (Vickers) come in separate oxygen concentrations, i.e. 24%, 28%, 35%, 40%. Other newer masks, i.e. Hudson, McGraw, Medi-shield, and Inspiron, use a facemask with a short "elephant trunk" hose attached to an interchangeable entrainment disc to allow a range of concentrations. The oxygen flow rate is set at 6-8 L/min depending on the FIO_2 chosen, entraining room air to give a resultant total flow rate of 40-60 L/min. Since room air is entrained, the use of a humidifier is not essential. The high-flow system also eliminates rebreathing and the need for a tight fit to the face. However, these masks may not deliver the intended FIO_2 if severe dyspnoea is present. The large PIFR in such patients may exhaust the reservoir in the newer, smaller volume masks, leading to the FIO_2 being lower and fluctuant. This is overcome by increasing the oxygen flow rate to 12-14 L/min (to give total inspired gas flows over 60 L/min).

2. *Low-flow Spontaneous Breathing Circuits*

These include anaesthetic circuits and circuits to deliver continuous positive airway pressure (CPAP) or spontaneous PEEP. These circuits incorporate a reservoir bag to deliver an FIO_2 set by the fresh gas mixture via an endotracheal tube or airtight mask.

B. Variable Performance Systems (FIO_2 depends upon oxygen flow, device factors and patient factors)

1. *No Capacity System*

Nasal catheter at low flow rates (less than 2 L/min). Hence there is insufficient oxygen storage in the airway during the expiratory pause to significantly affect the next inspiration. FIO_2 then depends upon the added oxygen flow rate and the peak inspiratory flow rate. In order to maintain the sam FIO_2, the added oxygen flow rate will need to be altered with each change in peak inspiratory flow.

2. *Small Capacity System*

(a) *Nasal catheters at high flows*

Significant oxygen storage occurs during the expiratory pause and varies with the length of the pause. Together with the breath-to-breath variation of PIFR, FIO_2 thus varies with ventilation. Moreover, major differences in alveolar oxygenation occur between mouth breathers and nose breathers, with a lower alveolar oxygen percentage found with the former group. The high flow rates may cause discomfort and drying of nasal mucosa. Nasal catheters are, however, cheap and easy to use, and the patient is able to eat or drink with them in situ. CO_2 rebreathing does not occur.

(b) *Simple, semi-rigid plastic masks* (i.e. MC, Edinburgh, Harris, Hudson)

Since some CO_2 rebreathing occurs, especially at low flows, the oxygen flow rate should be set at 4 L/min or greater. FIO_2 varies with patient ventilation and the oxygen flow rate (Table 5). A maximum concentration of only 60-70% oxygen is achieved by these masks. The tables of FIO_2 for these simple masks should only be used as guidelines. Large discrepancies between the delivered FIO_2 and that received by the patient (i.e. intratracheal FIO_2) occur with increasing rate and depth of breathing (i.e. increased PIFR). The standard oxygen flowmeter has a maximum flow rate of only 15 L/min and may not deliver adequate inspired oxygen. Special high-flow flowmeters or twin linked flowmeters are used in such a patient.

(c) *Tracheostomy masks*

These are small, plastic masks placed over the tracheostomy tube or stoma. The patient will inspire less oxygen than delivered, as dilution by room air occurs. Otherwise, they perform similarly to simple face masks.

(d) *T-piece circuit*

A T-piece is a simple, large bore, non-rebreathing circuit attached to an endotracheal or tracheostomy tube. Humidified oxygen is delivered through one limb of the T, and expired gas leaves via the other limb. The T-piece can be a fixed performance device if the fresh gas flow rate and the circuit volume are sufficient to provide for the patient's PIFR.

(e) *Face tent*

This is a large, semi-rigid plastic half-mask which wraps around the chin and cheeks. The oxygen mixture is delivered from the bottom of the mask, and gases are exhaled through the open, upper part. It is used to provide added humidification from a heated humidifier. Otherwise it has no advantages over the simple face mask.

3. *Large Capacity System*

Significant oxygen and CO_2 storage (i.e. rebreathing) occurs in these devices.

(a) *Soft plastic masks,* i.e. Pneumask, Polymask, Oxyaire. These masks have an added reservoir bag and thus a large effective dead space. FIO_2s greater than semi-rigid masks are possible, but considerable CO_2 rebreathing occurs if the oxygen supply fails or is reduced. They are potentially dangerous in patients without cardiopulmonary reserve and should be used with high oxygen flow rates. Rebreathing can be eliminated and delivered FIO_2 increased further if unidirectional valves are added, but asphyxia may occur in the unconscious patient if a valve become faulty.

(b) *Oxygen headbox, tents, cots and incubators* (see below).

Paediatric Oxygen Therapy

The PIFR of children, because of their smaller size, approximate more closely with the flow rate of oxygen delivery devices. Hence, higher FIO_2s are achieved. However, it is difficult to retain nasal catheters and masks on (especially restless) children. A single nasal catheter, placed at the level of the uvula and taped to the face, is well tolerated and is useful in infants and small children.

Oxygen Headbox or Hood

Oxygen is delivered into a box encasing the child's head and neck. The FIO_2 depends on the fresh gas flow, size of box, leak around the neck, head position, and how often the box is removed. It is a useful method in infants and small children, but high flow rates should be supplied and monitoring of oxygen concentration near the face is essential.

Incubator

Incubators provide oxygen as well as a neutral thermal environment. Patient access and recovery of oxygen concentration after opening the incubator are problems. The use of a headbox inside an incubator is common to give a more stable oxygen environment.

Oxygen Cot/Tent

Oxygen cots or tents may be used to nurse large children. Access, long recovery time for oxygen concentration and the difficulty to achievge high FIO_2s are problem.

Hazards of Oxygen Therapy

1. CO_2 Narcosis

When high oxygen concentrations are administered to patients with ventilatory failure who are dependent on a hypoxic drive, severe respiratory depression may occur, with loss of consciousness and, ultimately, death. This is seen particularly in patients with acute exacerbation of chronic bronchitis. Controlled oxygen therapy is needed in such cases. When patients are seen with CO_2 narcosis due to oxygen, the oxygen should not be withdrawn suddenly as a dangerous fall in PaO_2 will result. Such patients should be encouraged to breathe or, if unconscious, should be immediately ventilated.

2. Oxygen Toxicity

(a) *Neurological Effects (Paul Bert effects)*

Idiopathic epilepsy occurs with exposure to oxygen at more than 3 atmospheres absolute.

(b) *Lung Toxicity*

Pulmonary toxicity following exposure to high inspired concentrations of oxygen is a recognized clinical problem, but knowledge of the disorder remains limited. There is no specific pathological lesion, but progressive decrease in lung compliance occurs associated with the development of haemorrhagic interstitial and intra-alveolar oedema, and ultimately, fibrosis. The exact mechanism of the toxic effects of oxygen on the lung remains unknown, but it is generally thought that oxygen has a direct effect on lung tissue, affecting capillary endothelium before alveolar epithelium. A biochemical pathogenesis of oxygen-free radicals and hydrogen peroxide causing lung tissue injury has been suggested. Additional indirect factors that have been suggested include increased sympathetic activity, reduced surfactant activity, and absorption collapse. Differentiation of oxygen toxicity from other conditions of lung damage (i.e. ARDS) is extremely difficult, and the damage may be a common response to different types of injury.

It is generally agreed that oxygen pulmonary toxicity is dependent upon the duration of exposure and the concentration. However, precise details about "safe" periods of exposure and "safe" concentrations are unknown. Individual susceptibility to oxygen damage varies both within and among species. In patients with irreversible brain damage, ventilation with 100% oxygen produced changes in arterial oxygenation at 40 hours, and changes were reversible at this stage if the oxygen level was reduced to under 50%.

No damage was seen in volunteers breathing 50% for long periods, and no clinically relevant signs of toxicity appeared when 100% oxygen was used for less than 15-20 hours. Even when using high FIO_2s pulmonary toxicity does not always occur. The alveolar oxygen content or the FIO_2 appears to be more important, although the arterial tension (PaO_2) may modify oxygen tolerance. Damage in healthy lungs can occur, but whether the response is similar in lungs with pre-existing disease remains unclear. Patients with pulmonary injury may, paradoxically, be more resistant to oxygen toxicity. The converse may, however, be true. In general, clinical signs of toxicity (i.e. dyspnoea, substernal pain, deteriorating gas exchange and X-ray changes) are not normally detected with using oxygen less than 50% or 100% for short periods less than 24 hours.

(c) *Bronchopulmonary dysplasia,* a paediatric chronic lung disease originating in the neonatal period has similar abnormalities. This is seen when the immature lung is ventilated with high FIO_2s. Barotrauma is thought to be the major predisposing factor, but oxygen may accelerate the pathological process.

(d) *Retrolental Fibroplasia*

Blindness is caused by changes in retinal vessels. This occurs in premature babies under 1200 g weight (about 28 weeks) exposed to high oxygen concentrations, and relates to PaO_2 and retinal immaturity. Oxygen appears to stimulate immature vessels to vasoconstrict and obliterate, resulting in neovascularization, with haemorrhage, fibrosis, retinal detachment and blindness. PaO_2 should be kept between 50-80 mmHg (6.6-10.6 kPa).

Correct Clinical Use of Oxygen

Oxygen is a drug and has to be used correctly. It is given usually as a temporary measure to relieve hypoxaemia, but in no wat replaces the definitive treatment of the underlying cause. Oxygen therapy must be assessed by frequent measurements of blood gases and the alveolar-arterial oxygen gradient. PaO_2 must always be related to FIO_2 and the ventilation pattern. It is meaningless to quote the PaO_2 with no reference to the concentration or flow rate of oxygen. Finally, oxygen therapy must be *continuous not intermittent,* which may be harmful (with profound hypoxaemia).

In practice, oxygen administration for both adults and children over 50% should be given for as short a period as possible (except retrolental fibroplasia situations above), although when profound hypoxaemia is life-threatening (even 100%) concentrations should never be withheld. Conversely, restricting oxygen (using low concentrations) in hypoxic patients who are not oxygen sensitive is ignorant, stupid and dangerous. This is commonly seen with hypoxic patients who have raised $PaCO_2$, even though the hypercarbia is due to central depression from other causes (i.e. head injury or drug overdose) or neuromuscular failure (i.e. flail chest), and despite the hypoxia being profound. Other examples of this unfortunately common "asphyxia therapy" of rationing oxygen in hypoxia, is acute severe asthma (especially when the patient is hypocarbic), shock and sepsis. Hence, oxygen should never be restricted to hypoxic patients, except for those are sensitive (below).

1. Mild Hypoxaemia

Nasal catheters at 2-3 L/min or a simple mask at 4 L/min are suitable. If an oral (Guedel) airway is used, the nasal catheters must be placed inside the airway instead of the nares.

2. Moderate to Severe Hypoxaemia without CO_2 Retention

Example: when PaO_2 is approximately 50-60 mmHg (6.7-8.0 kPa). A simple mask is used with a flow rate of 4-15 L/min according to the PaO_2 and patient requirements. Extremely dyspnoeic patients with large PIFR will require oxygen delivered as high a flow as possible.

3. Hypoxaemia with CO_2 Retention

Controlled oxygen therapy with a venturi-type mask is used. A concentration of 24% is started, and blood gases are measured after 30-60 minutes. If the $PaCO_2$ is then below 75 mmHg (10 kPa), and if the rise in $PaCO_2$ is less than 10 mmHg (1.3 kPa), then the oxygen

is increased to 28%. Since these patients lie on the steep part of the oxygen dissociation curve, a small rise in PaO_2 will result in a relatively large increase in oxygen available to tissues. The FIO_2 may be increased further in the same way if hypoxaemia persists.

Nasal catheters at low flows may be used but are not ideal. At higher flows, controlled oxygen therapy cannot be achieved with these catheters.

4. Profound Hypoxaemia

Example: when PaO_2 is less than 50 mmHg (6.7 kPa). Mechanical ventilatory support is indicated. Continuous positive airway pressure (CPAP) by mask may be tried initially to avoid intubation. Positive end expiratory pressure (PEEP) may be used, to help reduce the FIO_2 being given.

Chapter 19: Acute Respiratory Failure in Chronic Obstructive Airways Disease

D. V. Tuxen

The term chronic obstructive airways disease (COAD) usually applies to chronic bronchitis and/or emphysema, but may also apply to largely irreversible airflow obstruction due to asthma, bronchiectasis or cystic fibrosis. Respiratory reserve is reduced, and superimposed acute respiratory failure (ARF) has significant morbidity and mortality. However, most precipitating factors of ARF are reversible, and the prognosis of patients who recover are good.

Aetiology

A number of factors may precipitate ARF in patients with COAD, including:

1. Acute Infection

This may be acute bronchitis or pneumonia. Acute bronchitis is precipitated by viral infection (with secondary bacterial invasion) or by primary bacterial infection. *S. pneumoniae* and *H. influenzae* are most common, but *S. viridans* and *Branhamella catarrhalis* may be found. Pneumonia is most commonly caused by *S. pneumonia* and *H. influenzae,* but mycoplasma, legionella and viral pneumonia are occasional causes.

2. Sputum Retention

Sputum retention may complicate COAD or ARF. Common causes are surgery, trauma, and depressed conscious level. The primary problem is failure of coughing to remove the increased secretion in COAD.

3. Bronchospasm

The relationship between bronchospasm in COAD and asthma is not always clear. Asthma itself may cause or coexist with COAD. In some patients, increased bronchial

reactivity may result from COAD. Precipitants of bronchospasm are similat to those of asthma.

4. Pneumothorax

The risk of pneumothorax is increased in COAD. ARF may be rapidly precipitated, depending on the size of the pneumothorax and the severity of the underlying lung disease.

5. Bullae

Large lung bullae may expand and precipitate ARF in a manner similar to pneumothorax. Occasionally, subpleural bullae may be mistaken for pneumothoraces.

6. Left Ventricular (LV) Failure

LV failure may result from coexisting ischaemic heart disease, fluid overload or biventricular failure secondary to cor pulmonale. COAD lungs are very sensitive to LV failure, and ARF may be precipitated even in the absence of obvious pulmonary oedema on chest X-ray.

7. Pulmonary Embolism

Pulmonary embolism is not commonly recognized as a cause of ARF in COAD, although it is found in 20-50% of autopsies. If it is not a primary cause of ARF, it may complicate other causes. It is often hard to diagnose, because of the pre-existing lung disease and the numerous possible causes of ARF in COAD. Interpretation of lung scans is difficult when COAD is present. A high index of suspicion is required, and pulmonary angiography may be necessary.

8. Uncontrolled Oxygen Administration

Uncontrolled oxygen therapy may precipitate acute hypercarbia in a small proportion of patients with more severe COAD, especially those with chronic hypercarbia. The consequent removal of the hypoxic drive to respiration is only a partial explanation. Major factors appear to be dissociation of CO_2 from haemoglobin by oxygen (Haldane effect), and worsening of ventilation-perfusion (V/Q) mismatch. The latter is probably due to reduction of hypoxic vasoconstriction in areas of shunt, allowing more CO_2 rich venous blood into the arterial circulation.

9. Sedation

Over-sedation can readily precipitate hypoventilation in severe COAD. Although this should reverse when the sedative effect wears off, sputum retention beforehand may result in persistent respiratory failure.

10. Endstage Lung Disease

Most precipitants of ARF in COAD are reversible, but COAD itself is commonly progressive, and may ultimately lead to death. The patient presents with apparent ARF from absent or trivial precipitating factors, and a long history of severe lifestyle limitation and refractory dyspnoea at rest.

Pathophysiology

Factors obstructing airflow in COAD include mucosal oedema and hypertrophy, secretions, bronchospasm, airway tortuosity and airflow turbulence, and loss of lung elastic recoil (due to loss of lung elastin and alveolar surface tension from alveolar wall destruction). Loss of lung elastic recoil leads to decreased expiratory airflow, because alveolar pressure (which drives expiratory airflow) and intraluminal airway pressure (which distends small airways during respiration) are reduced. Airflow obstruction results in prolonged expiration, pulmonary hyperinflation, increased work of breathing and the sensation of dyspnoea, all worsened during an exacerbation of COAD.

The pulmonary circulation is also abnormal in COAD. Alveolar distortion and destruction results in capillary bed loss, and hypoxia causes pulmonary artery vasoconstriction. These lead to pulmonary hypertension, secondary vascular changes, and ultimately, cor pulmonale. Increased hypoxia during ARF increases pulmonary artery pressure and may precipitate acute right heart failure.

The combination of airway obstruction, pulmonary parenchymal disease and circulatory disturbance leads to extensive V/Q mismatch. Underventilated lung areas act as partial or complete shunts. This results in arterial hypoxaemia, which when chronic, may cause secondary polycythaemia and increase pulmonary hypertension. Under-perfused or over-ventilated areas increase dead space. Thus, as a result of severe V/Q mismatch, ventilatory requirements for normocarbia are increased. Increased minute ventilation results in further increases in the work of breathing.

Since expiration is incomplete in airflow obstruction, this, with increased minute ventilation, result in permanent dynamic elevation of the functional residual capacity (FRC) or pulmonary hyperinflation. As lung volume is increased, the respiratory muscles (diaphragmatic and intercostal) become less efficient as a result of shortened fibre length and mechanical disadvantage, and the work of breathing is further increased. When the compromised inspiratory muscle capacity fails to meet the increased ventilatory requirements, chronic hypercarbia ensues.

Chronic hypercarbia is uncommon in COAD, and tends to occur late in the disease course, associated with renal acid-base compensation. It is usually seen in COAD dominated by chronic bronchitis with an FEV1 under 1 L, and is associated with polycythaemia, cor pulmonarle, and further CO_2 retention with uncontrolled oxygen administration. However, hypercarbic respiratory failure is readily precipitated by increased lung shunt. Patients with COAD have a poor response to increasing shunt. They have a limited capacity to increase minute ventilation, which may be decreased by the respiratory failure itself.

Clinical Features

ARF in COAD can present with two distinct clinical patterns.

1. Increasing Dyspnoea (the "can't breath" pattern)

This is more common, and results from impairment of airflow and gas exchange with no impaired respiratory drive. There is inability to achieve adequate ventilation despite a maximum ventilatory effort. Dyspnoea is accompanied by increased sputum, cough, wheezing, and reduced exercise tolerance. Hyperpnoea, use of accessory respiratory muscles, and pursed-lip breathing are usually present. Cyanosis and pulmonary hyperinflation may be evident. Rhonchi, prolonged expiration, and expiratory wheeze are usually auscultated. Signs of consolidation, usually at the lung bases, may be present if pneumonia or sputum retention are precipitating events. A loud pulmonary component of the second heart sound, sight ventricular (RV) heave (if not negated by pulmonary hyperinflation), elevated jugular venous pressure and peripheral oedema indicate pulmonary hypertension and cor pulmonale. In severe cases, right heart failure may be accompanied by tricuspid incompetence.

Respiratory muscle fatigue is initially manifested by impaited coughing and clearance of secretion, reduced tidal volume, and increasing respiratory rate. As fatigue progresses, abnormal breatinhing patterns may emerge, i.e. abdominal, alternating with rib cage breathing (respiratory alternans) and paradoxical indrawing of the abdomen on inspiration (abdominal paradox). Both fatigue and the consequent CO_2 retention may obtund conscious level. Features of CO_2 retention may be evident - warm dilated periphery, bounding pulse and sweating. Fatigue, abnormal breathing patterns and increasing CO_2 retention herald impending respiratory collapse.

LV failure or fluid overload may be indicated by cardiomegaly and upper lobe venous diversion on chest X-ray, audible chest crepitations, and a history of ischaemic heart disease. However, COAD can effectively mask the symptoms and signs of ischaemic heart disease and LV failure. Conversely, chest crepitations may occur in the absence of LV failure.

Pneumothorax or pulmonary embolism are suggested by sudden marked increases in dyspnoea. Asymmetrical respiration, abnormal percussion note and breath sounds, and tracheal and apex beat displacement suggest pneumothorax. Haemoptysis, pleuritic chest pain, pleural rub, an opacity on chest X-ray and evidence of a deep vein thrombosis in the legs point to pulmonary embolism.

2. Decreasing Dyspnoea (the "won't breath" pattern)

This less common form of ARF in COAD occurs when conscious level is depressed by drugs, illness, or excess oxygen administration. It is mimicked in the advanced stages of the "can't breath" group, when respiratory muscle fatigue and CO_2 narcosis have taken over. The primary problem is increasing hypercarbia and respiratory acidosis, with no increase in dyspnoea. A reduced central respiratory drive underlies the absence of increasing dyspnoea in response to a rising CO_2. However, an increased V/Q mismatch also contributes to the hypercarbia.

The sole initial feature may be the blood gas abnormalities; increased $PaCO_2$, acidaemia, and small fall in PaO_2. As failure worsens, clinical features become apparent. These include reduced respiration and dyspnoea, cyanosis, sputum retention, decreasing conscious level, and signs of hypercarbia. This is a more subtle presentation and a high index of suspicion and early blood gas measurement is required in these patients.

"Blue Bloaters" and "Pink Puffers"

The value of labelling patients as "blue bloaters" (mainly chronic bronchitis) and "pink puffers" (mainly emphysema) is uncertain, as the two disease processes usually co-exist, and the principles of management are similar. However, categorization of a patient, if clearly applicable, can be useful as the two types may have different clinical patterns and prognoses.

"Blue bloaters" - COAD patients dominated by chronic bronchitis have chronic cough, large sputum production, wheeze, fluctuating levels of dyspnoea, and severe V/Q mismatch. As a result, such patients are more prone to hypercarbia, CO_2 retention with oxygen administration, cyanosis, secondary polycythaemia, pulmonary hypertension and cor pulmonale. The tendency to cyanosis and peripheral oedema has resulted in the term "blue bloaters". The overall couse is often downhill, but recovery usually occurs from infection induced exacerbations.

"Pink Puffers" - Patients with COAD dominated by emphysema have a more constant level of dyspnoea with less cough, sputum, and wheeze. This disease process primarily affects pulmonary parenchyma with alveolar wall loss and little primary airway involvement. V/Q relationships tend to be better preserved, and less shunting occurs. Work of breathing and ventilatory requirements are increased, but with less shunting, increased respiratory effort (puffing) can normalize blood gases - hence the term "pink puffer". The course is characterized by gradually increasing dyspnoea until near terminal stages of the disease are reached. Thus, patients with emphysema presenting with respiratory failure are often closer to end-stage lung disease than those with chronic bronchitis.

Diagnosis and Assessment

Diagnosis of COAD

The diagnosis of COAD is usually established prior to patient presentation with respiratory failure. It is based on the following:

1. History of smoking or other causative factors.

2. Chronic cough and sputum production.

3. Longstanding dyspnoea with or without wheeze.

4. Lung function tests demonstrating largely irreversible airflow obstruction.

(a) Spirometry - shows a reduced FEV1/forced vital capacity (VC) ratio compared with predicted values. These values may improve to a small degree but not normalize with

bronchodilators. VC is initially normal and becomes reduced later in the course of the disease, but to a lesser degree than the FEV1.

(b) Flow-volume curves - demonstrate reduced expiratory flow rates at various lung volumes.

(c) Lung volumes - measured by helium dilution or plethysmography show elevated total lung volume, FRC, and residual volume.

(d) Carbon monoxide uptake - is a measurement of alveolar surface area, and its reduction approximates the amount of emphysema present. It may be normal or near normal in pure chronic bronchitis.

(e) Bronchial reactivity tests - such as histamine, methacholine, cold air or antigen challenge are occasionally used to see if there is a component of "asthma" present. A positive test suggests benefit from aggressive bronchodilator or steroid therapy.

Diagnosis of Respiratory Failure

An exacerbation of COAD is usually clinically obvious. However, it is important to diagnose the extent of deterioration. The following assessments may be useful:

1. Arterial Blood Gases (ABGs)

ABGs are mandatory to assess hypoxia, hypercarbia and acid-base status. The large majority of COAD patients are not chronically hypercarbic and will only develop hypercarbia when compensatory mechanisms are exhausted. Such patients will have normal bicarbonate levels, and the occurrence of hypercarbia signals possible respiratory collapse. Chronic hypercarbia may be recognized by a high bicarbonate level (over 30 mmol/L) and a base excess over 4 mmol/L (indicating renal compensation). However, other causes of raised serum bicarbonate need to be excluded (i.e. diuretic and high-dose steroid therapy or gastric fluid loss). Renal compensation will increase the serum bicarbonate by approximately 4 mmol/L for each 10 mmHg (1.33 kPa) of chronic PCO_2 rise above 40 mmHg (5.3 kPa).

2. Spirometry

This should be performed if possible, as it will indicate the severity of illness and deterioration, and provide a baseline measurement for subsequent assessments.

3. Chest X-ray

Chest X-ray is mandatory to diagnose or exclude pneumothorax, lobar or segmental collapse, pneumonia or obvious LV failure. The film will commonly show hyperinflated lung fields, low flattened diaphragms, and paucity of lung markings. Pulmonary hypertension is manifest by enlarged proximal and attenuated distal vascular markings, and by RV and atrial enlargement. Lung bullae may be evident.

4. Electrocardiogram

ECG is commonly normal, but may show features of right atrial or RV hypertrophy and RV strain, including P pulmonale, right axis deviation, dominant R waves in V1-2, right bundle branch block, and ST depression and T wave flattening/inversion in V1-3. These changes may be chronic or develop acutely. The ECG may also show co-existant ischaemic heart disease.

5. Sputum Microscopy and Culture

Although expectorated samples do not always reliably identify lower respiratory pathogens, sputum samples in COAD will usually culture the causative organism and guide antibiotic therapy.

6. Full Blood Count

Full blood examination may show polycythaemia. An elevated white cell count may indicate infection.

7. Theophylline Assays

Serum theophylline levels should be performed on patients receiving theophylline derivatives.

Differential Diagnoses

It is important to recognize or exclude less common causes of ARF in COAD which require specific therapy.

1. Left Ventricular Failure

LV failure may be clinically subtle. Minor pulmonary oedema and pulmonary venous congestion may precipitate respiratory failure in a severely compromised lung without clinical or radiological features of pulmonary oedema. Comparison with previous chest X-rays is important.

2. Pulmonary Embolism (PE)

PE should be suspected in any unexplained deterioration, especially where factors predisposing to deep venous thrombosis exist. Investigative lung scans and anticoagulant therapy follow conventional practice.

3. Pneumothorax

This may be difficult to detect clinically but is usually obvious on chest X-ray. However, careful X-ray inspection is required. A lung edge may not always be visible, and with a small pneumothorax, asymmetry of lung markings or apical density may be the only

clues. When dount exists, repeat chest X-rays with both inspiratory and expiratory views should be obtained.

4. Upper Airway Obstruction

Upper airway obstruction from any cause may mask the usual presenting symptoms of ARF. Unexplained deterioration, stridor, or voice alteration are important clues. Upper airway X-rays and tomograms, inspiratory/expiratory spirometry, flow-volume graphs, and direct or indirect laryngoscopy are performed when indicated.

Management

A. Conservative Measures

1. Oxygen

Most patients with COAD will not develop CO_2 retention from oxygen administration. It is more common in patients with severe COAD who are in respiratory failure. However, reversal of hypoxia is important, and oxygen should not be withheld if hypercarbia is present, nor withdrawn if it worsens. Oxygen is given initially by low-flow intranasal cannulae of 24% or 28% venturi mask. Oxygen therapy is best controlled by titrating delivery to achieve a saturation (SaO_2) of 90-92% measured by pulse oximeter and frequent ABGs. A rise in $PaCO_2$ with oxygen administration is common, and should be expected. If the rise is excessive (i.e. over 10 mmHg or 1.3 kPa), delivered oxygen is reduced, titrating SaO_2 to 2-3% below the previous value, and ABGs repeated. If no $PaCO_2$ rise occurs with oxygen therapy, a higher SaO_2 may be targeted with repeat ABGs. If hypoxia is inadequately reversed (i.e. SaO_2 <85%) higher oxygen delivery systems should be used.

2. Bronchodilators

Bronchodilators are routinely given in all exacerbations of COAD, because a small reversible component to airflow obstruction is common, and bronchodilators improve mucociliary clearance of secretions. Nebulized beta-2 sympathomimetics (i.e. salbutamol, terbutaline, or fenoterol) are given 2-4 hourly. Combination with ipratropium bromide augments efficacy. Aminophylline (loading dose 5.6 mg/kg IV over 30 min, followed by infusion 0.5 mg.kg/h) is also commonly given, despite doubts on its overall benefits. Theophyline has the additional benefit of improving diaphragm contractility, although the clinical importance of this is not yet clear. Parenteral sympathomimetic agents are rarely indicated and not recommended for routine use.

3. Steroids

Short term steroids may improve airflow obstruction in an exacerbation of COAD, but not in every patient. They should be avoided if ARF is due to bacterial pneumonia or bronchitis. Doses used are similar to those for acute asthma (i.e. IV hydrocortisone 3 mg/kg or methylprednisolone 0.5 mg/kg given 6 hourly for 72 hours).

4. Antibiotics

Benefits of antibiotic therapy are conflicting. Antibiotics are likely to benefit only those exacerbations due to bacterial infection. Nonetheless, it is reasonable to initially administer antibiotics until bacterial infection is confirmed or excluded. Suitable antibiotics to cover common bacterial pathogens are amoxicillin, erythromycin or a third cephalosporin.

5. Non-Invasive Secretion Clearance

Clearance of lower respiratory secretions is of crucial importance.

(a) *Chest Physiotherapy* is the primary technique, and should be initiated and regularly repeated as both a curative and preventative measure. Encouragement of coughing and deep breathing are the two most important factors.

(b) *Nebulized Mucolytic Afents* such as acetylcysteine have been proposed as adjuncts to bronchodilators, but their benefits are uncertain.

6. Other Measures

Other adjunctive measures are applicable to some patients.

(a) *Hydration, Diuretics, Digoxin and Vasodilators.* COAD patients are sensitive to changes in fluid status, and intravenous rehydration should be undertaken cautiously. Diuretics and digoxin are beneficial in LV failure. Even if evidence of LV failure is minimal, a trial of diuretic is worthwhile in refractory cases. Diuretics will reduce fluid overload in cor pulmonale. However, they should be used with care in those with severe pulmonary hypertension. Excessive decrease in preload will decrease RV filling pressure and may result in a low output state. Digoxin is of no established benefit in cor pulmonale, as the primary problem is one of afterload. Pulonary vasodilators have a more rational basis, but clinical results are conflicting, without clear benefits. They may even be detrimental, and are not generally used.

(b) *Heparin* given subcutaneously in low doses (i.e. 5000 units SC bid) is recommended as a prophylactic measure against venous thrombosis and pulmonary embolism.

(c) *Electrolyte Correction* is undertaken. Hypophosphataemia is common, and hypomagnesaemia, hypocalcaemia, and hypokalaemia may also present and also impair respiratory muscle function. Hyponatraemia may occur with inappropriate antidiuretic hormone release or with excess use of diuretics.

(d) *Intercostal Drainage* is indicated for pneumothorax and pleural effusions of sufficient volume to compromise respiratory function. Instead of conventional drains, simple aspiration using a fine cannula, 3-way tap and syringe, have resulted in reduced complications, admission rate, and hospital stay.

(e) *Respiratory Stimulants* increase respiratory drive and lower $PaCO_2$. These include acetazolamide, medroxyprogesterone, naloxone, doxapram and almitrine. The principle of using such drugs is doubtful in COAD, where respiratory drive is already increased (the "can't breathe" group). These drugs also significantly increase respiratory work, respiratory distress and risk of fatigue. Sustained benefits have not been demonstrated for most agents, and they are not generally recommended. They may have limited application in the "won't breathe" group, especially those patients associated with sedation or anaesthesia. Narcotic induced respiratory depression is most appropriately managed with naloxone. Other forms of respiratory depression may be managed with doxapram, which acts both on peripheral carotid chemoreceptors and respiratory centre. However, the V/Q mismatch which contributes significantly to hypercarbia, will greatly limit the capacity of a respiratory stimulant to reduce $PaCO_2$.

Almitrine is believed to act by sensitizing peripheral chemoreceptors to both hypoxia and hypercarbia. It is believed to reduce $PaCO_2$ both by stimulating respiration and improving V/Q mismatching (by augmenting hypoxic vasoconstriction in hypoxic areas and redistributing pulmonary blood flow). Some studies have shown benefit in exacerbation of COAD but use of almitrine is yet to be established.

(f) *Nutrition* is important as malnutrition is associated with decreased respiratory muscle mass and strength, and increased risk of fatigue, ARF, and death. Enteral feeding is preferred, but parenteral nutrition is given in gastrointestinal dysfunction. Excessive calories and glucose increase CO_2 production, and should be avoided.

B. Non-Conservative Measures

1. Invasive Techniques for Sputum Clearance

Most of these are temporizing techniques applied to patients who have failed or are expected to fail with non-invasive sputum clearance techniques. The aim is to avoid intubation and mechanical ventilation if possible.

(a) *Oropharyngeal/Nasopharyngeal Suctioning.* It is uncommon for the tip to reach the trachea, but the procedure is useful in clearing pharyngeal secretions, stimulating coughing and clearing lower respiratory secretions coughed only as far as the hypopharynx.

(b) *Nasopharyngeal Airway* allows the passage of the suction catheter through the nose and upped pharynx towards the larynx.

(c) *Fibreoptic Bronchoscopy* guarantees lower airway entry and access to all major subsegments. Although effective in clearing sputum, it is very labour intensive. It is usually indicated by focal collapse or consolidation due to obstruction by sputum plug.

(d) *Minitracheostomy* involves insertion of a small diameter (4.0 mm) tracheostomy tube through the crico-thyroid under loca anaesthesia, using the Seldinger technique. It allows suctioning using a fibe bore (10 FG) catheter. The tracheostomy is left patent at all times, to allow ventilation through the tube as well as the mouth and nose.

(e) *Endotracheal Intubation* solely for lower airway suction, (without ventilatory support) may be questioned, but has been used. It is less well tolerated than mini-tracheostomy, but provides wide bore suction access and better control of inspired oxygen and humidity. Ventilatory support is easily instituted if required.

(f) *Formal Tracheostomy* provides the best, most comfortable and most stable form of wide bore lower airway access.

2. Mechanical Ventilatory Support

When respiratory failure progresses or fails to resolve despite aggressive conservative treatment, intubation and mechanical ventilatory support becomes necessary. The decision to ventilate requires careful consideration. Mechanical ventilation is associated with weaning difficulties and ventilator dependence. Hypercarbia or acidosis alone are not indications for mechanical ventilation, as they can be sustained for some time without impending respiratory collapse. As with acute asthma, the decision is based on a number of criteria:

(a) The clinical appearance of fatigue and impending respiratory collapse.

(b) Increasing $PaCO_2$ despite adequate conservative treatment, and not due to oxygen administration.

(c) Deteriorating conscious state due to fatigue, hypercarbia or both.

(d) Hypoxia, refractory to high levels of inspired oxygen.

(e) Deterioration due to failure of sputum clearance.

(f) Respiratory arrest.

Mechanical ventilation is withheld in endstage disease, when permanent ventilator dependence is likely. This decision should be based on certain criteria. In general, patients must fulfil all criteria below for ventilation to be withheld.

(a) Known severe, fully assessed COAD which has failed to respond to adequate therapy.

(b) Known or suspected chronic respiratory failure.

(c) Severe limitation by dyspnoea with a poor "quality of life".

(d) No identifiable reversible factors.

Mechanical Ventilation Technique

Ventilatory strategies aim to minimize pulmonary hyperinflation by use of low tidal volumes, low minute ventilation, and long expiratory times. Tidal volumes of 10-12 mL/kg are commonly recommended, but 8-10 mL/kg may be better. Although controversial, a high

inspiratory flow rate is recommended as it results in a short inspiratory time, and hence a longer expiratory time for the given ventilatory rate. It has been shown to reduce pulmonary hyperinflation and alveolar pressure and to improve gas exchange. Ventilator rate must be adjusted to achieve a low minute ventilation. Minute ventilations of less than 200 mL/kg are guidelines, and if used with small tidal volumes (8-10 mL/kg), allow relatively high ventilator rates (up to 20-25/min). If high minute ventilations are required to normalize pH, the degree of pulmonary hyperinflation and its effects should be determined beforehand. If pulmonary hyperinflation is excessive, minute ventilation should not be increased, and hypercarbic acidosis is accepted. Positive end expiratory pressure (PEEP) increases pulmonary hyperinflation and risks hypotension and should not be applied.

If controlled hypoventilation is not required, then a ventilator support mode must be chosen. This has been the subject of much debate. Intermittent mandatory ventilation (IMV) is preferred by many, although it has no advantage over controlled ventilation in terms of duration of ventilation or outcome. It has the theoretical advantage of promoting ongoing respiratory muscle activity to minimize wasting, and it does not allow large, patient-induced increases in minute ventilation.

Continuous positive airway pressure (CPAP) either by face mask or endotracheal tube has been proposed to overcome intrinsic PEEP. This has the theoretical advantage of reducing work of breathing, and may be tried either during partial ventilator support (i.e. IMV) or as an alternative to mechanical ventilation. Its role in COAD ARF is yet to be established. Jet ventilation at 100 breaths/min can achieve satisfactory gas exchange in patients with COAD, but advantages over standard ventilatory techniques have not been shown. Newer modes of flow-by and pressure support also have theoretical advantages of reducing work of breathing and promoting a better ventilatory pattern, but have not yet been fully investigated.

Weaning

Weaning a patient with severe COAD from ventilatory support can be difficult and prolonged. Numerous criteria have been proposed to assess the capacity of the patient for weaning (Table 1). None are absolute in their predictive accuracy, and weaning nearly always depends on clinical assessment as ventilatory support is reduced. Various modes have been proposed to facilitate weaning, including IMV, pressure support, CPAP, and flow-by ventilation. No method has been consistently shown to accelerate the weaning process. It must be suspected that the major determinant weaning is recovery from the precipitating illness, and not the ventilatory technique.

Prognosis

Most patients with COAD who present with ARF do not have end stage disease. Although their acute illness may be life threatening, their short and long term outcome is often good. Martin reported 36 patients with exacerbation of COAD, and found 96% hospital survival and 72% 2-year survival; only 1 patient required mechanical ventilation. Although most patients do not require mechanical ventilation, of those ventilated, the hospital survival rate is 80%, and 2-year survival significantly lower at 30%.

Table 1. Indicators for Weaning from Mechanical Ventilation in COAD

Sahn et al

Minute ventilation requirement < 10 L/min
Ability to double this on command
Spontaneous respiration rate < 20 breaths/min
Maximum inspiratory pressure > 20 cm water

Tahvanainer et al

Maximum inspiratory pressure > 25 cm water
Vital capacity > 10 mL/kg
SaO_2 > 90% on 40% inspired oxygen

Chapter 20: Acute Upper Respiratory Tract Obstruction

P. D. Cameron

Acute progressive upper respiratory tract obstruction is a life threatening emergency. Possible causes of airway obstruction in an emergency room or Intensive Care setting are many. Diagnosis must be made quickly and therapy immediately directed towards securing a patent airway.

Aetiology

The upper airway commences at the nose and lips, and continues through the oral and nasal pharynx, larynx, carina, and main stem bronchi to the origin of the major divisions. Functional and mechanical causes for obstruction may occur from within the lumen, in the wall, or extrinsic to the wall of an anatomical or artificial airway.

Table 1 lists some clinical conditions which may be associated with acute upper airway obstruction. Adult epiglottitis has been recognized with increasing frequency in recent years and appears to carry a greater mortality than the childhood variant. Some chronic conditions may progress rapidly to an acute phase, i.e. tumour haemorrhage, tissue oedema, and altered conscious state.

Diagnosis

The opportunity to diagnose the cause of an acute obstruction, by taking a careful history and making a physical examination, occurs only infrequently. Undue attention must not be directed towards establishing a cause, away from the more urgent need of establishing a clear airway.

Clinical Presentation

Early symptoms and signs of airway obstruction may be few; dyspnoea only becoming evident on impairment of gas flow during episodes of exercise-induced tachypnoea. Late signs

of obstruction and respiratory decompensation may be brief in onset, and soon progress to complete obstruction, when extreme anxiety and agitation are usually marked in conscious patients. Gasping inspirations, dysphagia, persistent cough, use of respiratory accessory muscles, nasal flaring, suprasternal and intercostal tissue retraction, cervical ecchymosis and subcutaneous emphysema, absence of the thyroid cartilage prominence, paradoxical chest wall movements and easily audible stridor may all be indicators of partial airway obstruction. If phonation and cough are lost, the patient may use the international distress sign and clutch his throat between thumb and index finger to signal his distress. Cyanosis, diminishing stridor, protective posturing, diaphoresis, acidosis, and loss of consciousness are very late signs of hypoxaemia and hypercarbia, and often herald the onset of terminal cardiac dysrhythmias.

The clinical setting fo the patients may give some guide to the aetiology of an obstruction (Table 1). Patients can progress to acute obstruction following certain therapeutic modalities, i.e. postoperative haemorrhage and oedema, and drug- or food-induced angio-oedema.

Physical examination should include an inspection of the oral cavity (in unconscious patients particularly, but avoid instrumentation in suspected epiglottitis) and auscultation over the larynx, trachea, and lung fields. It is important to exclude tension pneumothorax and flail chest, which may mimic some features of obstruction. In a subacute setting, use of accessory muscles, the ability to phonate and cough, and the degree and nature of stridor should be regularly checked, to detect clinical deterioration and increase in the work of breathing. Stridor may be inspiratory (denoting supraglottic obstruction), expiratory (obstruction below the glottis), or both, and in adults usually signifies an airway diameter of 5 mm or less. Hypertension and tachycardia may reflect hypercarbia, hypoxaemia, and acidosis. Partially obstructed patients should not be sent unaccompanied for additional diagnostic tests (i.e. to a radiology department). Recumbency may precipitate complete obstruction.

Special Investigations

A more exact localization and characterization of the obstruction may be made with special tests. If time permits, a diagnostic workup should include neck and chest X-rays (anteroposterior and lateral views), airway tomography, CT scans, arterial blood gas estimation, pulmonary function testing, and bronchoscopy. Clinical features of respiratory failure from small airway obstruction (i.e. asthma) may mimic some aspects of upper aiway obstruction. Time should not be wasted in making the sometimes difficult differentiation between the two (by evaluation of flow-volume loops) before management principles are enacted.

Management

Although a diagnosis may be incomplete, general principles of resuscitation should be directed towards relieving the obstruction and increasing the available inspired oxygen. Early surgical consultation is advisable. Specific management options will depend on the particular cause and severity of obstruction and the location of the patient. In any case, the patient should be continuously observed.

1. Unconscious Patient

The presence of a pulse and spontaneous respiratory efforts is determined; if absent, cardiopulmonary resuscitation is started. Lingual obstruction is relieved by anterior displacement of the mandible and extension of the head on the neck (if no cervical spine injury is suspected). Any oropharyngeal debris is evacuated, and the patient is positioned slightly head-down and semi-prone. Oropharyngeal or nasopharyngeal artificial airways may be needed. Endotracheal intubation may follow on a semi-elective basis. An intravenous line should be established, and ECG monitoring commenced.

2. Oxygen

Oxygen is given by facemask, and positive pressure ventilatory assistance by a self-inflating bag-valve device (i.e. Air Viva or Laerdal resuscitators) may be required. Humidification is desirable in order to avoid the accumulation of dried secretions.

3. Complete Obstruction

The Heimlich manoeuvre may be applied if an aspirated foreign body (mostly radiolucent) is markedly compromising the airway of a conscious or unconscious patient (i.e. "Cafe Coronary" syndrome). Repeated upper abdominal thrusts are alternated with interscapular back blows and, if necessary, mouth-to-mouth ventilation. Digital evacuation of a proximally dislodged obstruction from the oral cavity may be successful in restoring the airway. This manoeuvre is not performed in a patient who can still breathe; if improperly performed, the procedure may be hazardous (i.e. in children or pregnancy).

(a) *Tracheostomy* as an emergency means of securing an airway, is rarely required.

(b) *Cricothyrotomy* ("minitracheostomy") is a safer procedure by non-surgeons, until a formal tracheostomy can be completed to bypass a glottic or supraglottic obstruction. A small diameter endotracheal tube (i.e. Portex "Mini Trach") can be inserted through a midline incision in the relatively avascular cricothyroid membrane.

(c) *Transtracheal ventilation* via cricothyroid membrane puncture using a large bore intravenous cannula, 3 mL syringe, and an endotracheal tube adaptor connected to an anaesthesia bag or oxygen source, is also a satisfactory emergency technique. However, this technique should only be used if adequate expiration is judged feasible.

4. Endotracheal Intubation

Except in an absolute emergency, endotracheal tube placement should only be attempted by a skilled clinician under optimum conditions. A review of the patient's case notes may reveal useful information concerning previous intubation. Adequate suction, skilled assistance, a range of endotracheal tube sizes, and resuscitation equipment must be available. The procedure should preferably be undertaken in an operating room with an experienced surgeon prepared to perform immediate tracheostomy. A prudent approach is to intubate the patient awake, unpremedicated, and fasted, using a fibreoptic intubating laryngoscopy or bronchoscope, following pre-oxygenation, topical anaesthesia (including by nebulization) and

cricoid pressure. However, the patient may be too restless, and awake intubation may not be possible.

An inhalation induction of anaesthesia with nearly 100% oxygen (or helium/oxygen) is then preferable to the of intravenous hypnotics and muscle relaxants, in order to maintain a spontaneously breathing patient with some airway protective reflexes. In this way, direct visualization of the airway may also be possible, with additional guidance gained from the origin of airway secretion bubbles in the vicinity of oedematous mucosa and a distorted epiglottis. This is particularly so for laryngotracheal disruption, epiglottitis, airway oedema or burns, and tumours. Use of a translaryngeal bougie, fibreoptic stylet or percutaneous retrograde (cricothyroid) guide wire may permit intubation in the presence of proximal visual obstruction.

In difficult cases, epiglottic contact and suspension by a straight bladed laryngoscope or rigid bronchoscope may be indicated, although this carries some risk of haemorrhage or epiglottic fragmentation. Continuous oxygen insufflation into the hypopharynx may provide a lesser risk of hypoxia during instrumentation. Monitoring oxyhaemoglobin saturation with pulse oximetry is highly desirable.

Once endotracheal intubation is safely accomplished, a tracheostomy may then be performed if considered necessary. Secure fixation of the endotracheal tube is mandatory. The upper limbs of the patient may need to be secured if necessary, to avoid self-extubation. Extubation should be undertaken when the patient is awake, capable of competent laryngeal reflexes and an air leak exists around the tube with the cuff deflated. Facilities for emergency reintubation should be immediately available.

5. Bronchoscopy

Fibreoptic bronchoscopes have reduced some of the risks of emergency intubation, and have facilitated making an early diagnosis. Rigid bronchoscopes are, however, preferred for the removal of foreign bodies.

6. Pharmacological Adjuncts

Drug therapy may be required in certain clinical situations of upper aiway obstruction (Table 2).

7. Helium-Oxygen Mixtures

Helium-oxygen mixtures with a density less than air, may improve gas flow past airway obstruction and decrease the work of breathing. Helium (40%) with oxygen can substantially improve arterial blood gases.

8. Extra-corporeal Membrane Oxygenation

Extra-corporeal membrane oxygenation (ECMO) has been used in the emergency and perioperative support of airway-obstructed patients requiring major surgery on the trachea and

mainstem bronchi. Preoperatively, following heparinization, perfusion catheters are peripherally inserted into the vena cava and aorta.

Additional Considerations in the ICU

1. Elderly, debilitated, or obtunded patients have diminished airway protective reflexes and may require parenteral rehydration and nutrition.

2. It is safer to change tracheostomy tubes over steriles suction catheters, to avoid the creation of false passages.

3. Blunt trauma to the larynx and trachea is frequently overlooked in the presence of more obvious injuries. A cause must be found for cervical and thoracic subcutaneous emphysema. Cervical spine injury is not infrequently found in association with tracheal/laryngeal injury.

4. Endobronchial intubation may isolate a healthy lung from intrapulmonary haemorrhage and obstructive clot formation.

5. Usually benign tracheal stenosis may be exacerbated by intercurrent infection-induced mucosal oedema.

6. Pulmonary oedema may follow maximum inspiratory efforts against an obstructed airway, particularly in children, or may follow the relief of epiglottitis.

7. patients with airway burns should be intubated sooner rather than later, as mucosal oedema may progress over 24 hours. Tracheostomy in these patients is associated with a 50% mortality (due to sepsis).

8. Wire cutters should be at the bedside of a patient with interdental wiring to facilitate rapid opening of the mouth, should postoperative airway obstruction occur.

9. Laryngoscopy may rupture a tonsillar or retropharyngeal abscess and cause pulmonary soiling. Drainage under local anaesthesia in an awake patient, properly positioned, is preferable.

10. Although a chronic problem, obstructive sleep apnoea is sometimes monitored in the ICU. Nasopharyngeal airways commonly employing continuous positive airway pressure, may provide temporary relief until more definitive diagnosis and therapy can be undertaken.

11. Early airway protection in adult epiglottitis is advisable, particulary if bacteraemia is evident. Antibiotic therapy is directed against the most likely pathogens (*Haemophilus influenzae* and *parainfluenzae, Streptococcus pneumoniae, Staphylococcus aureus* and *haemolytic streptococci*). Systematically administered steroids may ameliorate associated mucosal oedema.

12. More specific therapies for paediatric problems and anaesthesia related problems, are best sought from an appropriate text.

Summary

Failure to diagnose and adequately treat acute airway obstruction makes other resuscitative therapies futile. A better prognosis may be expected by rapidly instituting first aid measures (positioning and oxygenation) for a compromised airway. It is then generally safer to await skilled assistance rather than embark on any unfamiliar procedure which may prove more hazardous for the patient.

Chapter 21: Endotracheal Intubation and Tracheostomy

N. J. Davis

The provision of an artificial airway by tracheal intubation is frequently required in Intensive Care, especially in patients with impaired laryngeal reflexes or who are in acute respiratory failure. Intubation of the trachea is possible with an orotracheal, nasotracheal or tracheostomy tube.

Endotracheal Intubation

The major indications for intubation in the Intensive Care Unit are:

1. To secure or maintain a clear airway.

2. To prevent aspiration of gastrointestinal tract contents.

3. To enable adequate tracheal suction.

4. To apply mechanical ventilatory support.

5. As a means for delivering high concentrations of oxygen.

Tracheal intubation is performed through either the oral or nasal route. There is division of opinion as to which is the better method. The main advantages of nasal intubation are:

1. A nasal tube is usually better tolerated by patients.

2. It is easier to intubate via the nasal route in the awake patient.

3. A nasal tube is easier to fix and secure to the patient.

4. Nasal intubation avoids tube occlusion or damage by the patient's teeth.

Unfortunately, nasal intubation has the disadvantage that smaller diameter tubes are required. Tracheal suctioning is thus more difficult, and there is an increased likelihood of tube occlusion. Airway resistance is also considerably greater in spontaneous breathing, and weaning off mechanical ventilatory support may be delayed. There is a further risk of causing

damage to nasal passages and nose bleeds can be precipitated. Bacteraemia has also been shown to occur more frequently with nasal than with oral intubation.

The intensivist should be familiar with the various techniques of tracheal intubation. The procedure may be performed in the awake patient (with or without local analgesia and sedation) or after intravenous administration of an induction agent (i.e. diazepam or thiopentone) and a muscle relaxant (usually suxamethonium). If respiratory obstruction is present, muscle relaxants should be avoided. Preoxygenation with 100% oxygen for several minutes must be carried out prior to the procedure.

The Difficult Intubation

Difficulties with endotracheal intubation can be anticipated in patients with:

1. a short muscular neck with a full set of teeth;

2. a receding lower jaw;

3. a long, high curved palate;

4. limited neck and jaw movements (i.e. as a result of osteoarthritis and trismus) and;

5. space occupying lesions in the pharynx and larynx.

When a difficult intubation is anticipated, awake intubation can be performed using a fibreoptic bronchoscope or a fibreopetic laryngoscope. Other methods such as "blind" intubation or retrograde catheter insertion should not longer be necessary. It must be stressed, however, that the intensivist must be familiar with the technique before attempting to use fibreoptic instruments for difficult intubations.

Endotracheal and Tracheostomy Tubes

Orotracheal, nasotracheal and tracheostomy tubes should be regarded as foreign bodies within the airway. Since they always cause microscopic lesions of the mucosa (and sometimes significant gross lesions), careful consideration should be given to the types of tubes used in Intensive Care.

Tube Material

Early red rubber tubes have no place in an Intensive Care Unit. Only tubes made of non-irritant, implant-tested materials should be used. Disposable, plastic polyvinyl chloride or silastic tubes are satisfactory. They are relatively kink resistant and offer better long-term tolerance.

Tube Shape

A conventionally shaped (curved) endotracheal tube will be deformed according to the airway anatomy and exert forces at the base of the tongue, posterior larynx, and anterior

trachea. The deformation forces are less with new flexible tubes and those tubes which conform more anatomically to the airway.

Tube Size

With translaryngeal intubation, a tube with an outside diameter considerably less than the diameter of the cricoid ring should be used, in order to diminish the risk of laryngeal damage (i.e. subglottic stenosis). The tube sizes recommended for men should have external diameters less than 13 mm, with internal diameters of 8-9 mm; and for women, 11 mm and 7-8 mm respectively. The diameter of a tracheostomy tube should also be much less than the internal diameter of the trachea. Tube sizes for children are discussed in Chapter 10, Equipment for Paediatric Intensive Care.

Tube Cuff

The stiff cuffs of red rubber tubes and older plastic tubes require fairly high pressures to overcome their stretch pressures. Hence, when such a cuff is inflated to obtan an adequate seal, excessively high intracuff and cuff-to-tracheal wall pressure result. Tracheal damage from endotracheal tube cuffs (such as ulceration, dilation, and stenosis) is a well recognized problem. Theoretically, the cuff-to-tracheal wall pressure should be considerably less than the capillary perfusion pressure of 32 mmHg (4.3 kPa), so that mucosal microcirculation is not arrested (although an even distribution of cuff pressure against the tracheal wall is also important).

Various cuff designs have been introduced to reduce cuff-to-tracheal wall pressure, including intermittently inflating cuffs, double cuffs, foam (Kamen-Wilkinson) cuffs, and cuffs consisting of sets of annular walls. The thin-walled, high-volume, low-pressure ("floppy") cuff is by far the most successful and widely used, and is recommended for Intensive Care patients. With this cuff, intracuff pressure equals cuff-to-tracheal wall pressure, and when the former is kept below 30 cm water (3.0 kPa), mucosal circularion is not seriously affected. The McGuiniss pressure-limiting pilot balloon (Lanz, USA) is a safety device to prevent overinflation of a large-volume cuff. Nitrous oxide will diffuse into an air-filled cuff and increase intracuff pressure and volume, and this should be rememberewd when Intensive Care patients undergo prolonged surgery with gaseous anaesthesia.

Endotracheal Tube Adaptors

Standardization of respiratory therapy equipment is important so that all connectors are compatible. Adaptors must allow manual disconnection to enable tracheal suctioning to be carried out. The use of 15 and 22 mm coaxial connectors reduces compatibility problems.

Long-Term Intubation

In general, endotracheal intubation is limited to a period of about 2 weeks. A tracheostomy should be avoided unless the need for the artificial airway exceeds this length of time, although there is still some controversy regarding this period.

Although intubation itself has a number of complications, many of which are avoidable, prolonged intubation avoids the complications of tracheostomy. However, the main disadvantages of long-term intubation are:

1. The need for adequate patient sedation in order to tolerate the tube.
2. The possibility of accidental extubation or misplacement into a main bronchus.
3. Laryngeal damage, which can be very serious. This is rarely a problem if proper tubes are used, and the intubation period limited to 2 weeks. Laryngeal oedema may be a problem following extubation.
4. Tracheal stenosis - this is now a rare problem with the use of low-pressure cuffs.

Care of the Intubated Patient

The tube must be well secured with the adaptor and ventilator hoses adequately supprted. Tapes, if used to secure the tube, should not be tied too tightly. Care should be taken to avoid skin abrasion around the mouth or venous occlusion of the neck, especially if intracranial hypertension is present. The tube should be marked where it emerges from the mouth or nose to enable displacement to be quickly detected. Mouth care is important regardless of whether an oral or nasal tube is used. The cuff should be kept inflated at all times. Intermittent deflation of the cuff offers no advantages. When it is necessary to change or reposition a tube, it is worthwhile to check the intracuff pressure after inflation (with an aneroid manometer) to avoid overinflation beyond 30 cm water (3.0 kPa).

Tracheostomy

Tracheostomy should not be embarked on lightly, because of the considerable morbidity as well as an associated mortality of approximately 3%. Nonetheless, the relative safety of the actual tracheostomy operation in critically ill patients has been demonstrated. In some circumstances, a cricothyroid minitracheotomy may be considered rather than formal tracheostomy. In general, the indications for tracheostomy are:

1. The need for an artificial airway for longer than 2 weeks.

2. Prolonged absence of laryngeal reflexes or the ability to swallow (i.e. after a cerebrovascular accident).

3. Considerable sputum retention. A tracheostomy may be needed for adequate tracheobronchial toilet.

4. Injuries to head and neck.

5. Upper airway obstruction. A tracheostomy is more commonly required in chronic obstructions above the trachea. An acute upper airway obstruction can nearly always be managed initially by endotracheal intubation. An elective tracheostomy may then be performed at leisure, if an indication arises.

6. Reduction of anatomical dead space was previously suggested as an advantage of tracheostomy but cannot be considered an indication.

Respiratory Failure

The operation of tracheostomy should in most instances be carried out in an operating theatre, with an endotracheal tube in situ. General anaesthesia is preferred but there are times when local analgesia may be justified. The need for "crash" tracheostomy is almost non-existent in centres where good care is provided by competent staff.

The actual operation is important. If the incision is made too high, damage to the larynx can result. It is extremely important never to damage the cricoid ring and the first tracheal cartilage, as subglottic stenosis is often a late complication. Tracheostomy should not be left for the inexperienced surgical trainee to perform without adequate supervision. An inverted U incision (Bjork flap) will facilitate replacement but is best avoided, as this may result in stenosis at the stomal site. Strong stay sutures should be inserted, as these can be lifted to enable reinsertion of the tube when required. The wound should be dressed with a dry dressing. Tracheostomy in children is discussed in Chapter 96.

Tracheostomy Tubes

As with endotracheal tubes, low-pressure, high-volume cuffs are used. The commonly used tubes are made of polyvinyl chloride (PVC), silastic, or metal. PVC and silastic tubes meet most clinical requirements. Metal tubes are usually used for long-term tracheostomy, especially when a cuff is not needed. The thin wall of the tube enables a changeable inner tube to be used. A correctly shaped tracheostomy tube should not exert pressure against the trachea posteriorly with its convex contour, nor direct its tip against the anterior tracheal wall.

Minitracheostomy

Minitracheotomy tubes (i.e. Portex "Mini Trach") are small diameter (4.0 mm), cuffless tubes inserted percutaneously through the cricothyroid membrane, after infiltration with local anaesthesia. Placement using the Seldinger technique of first inserting a guidewire and then inserting the tube with dilator over the wire is probably less traumatic. They are useful for suctioning lung secretions in patients with sputum retention, while avoiding endotracheal intubation or formal tracheotomy. Glottic function is maintained. The necessity for a small 10 FG suction catheter excludes its use in small children. These tubes may also be inserted in an emergency, in life-threatening, upper airway obstruction. Potential complications include haemorrhage, surgical emphysema, displacement, and inhalation of flangeless tube. Minitracheostomy tubes are contraindicated in acute respiratory failure and in comatose patients without a cough reflex, i.e. when orotracheal intubation or formal tracheostomy are necessary.

Connector

A swivel connector should be used to reduce movement at the tracheostomy site.

Speaking Tubes

As speaking is impossible with a cuffed tube, there are tubes designed to enable phonation with the cuff inflated. Many of these tubes use a separate gas flow which, when

required, is diverted into the trachea above the cuff and through the larynx. The spontaneously breathing patient can also be enabled to speak during exhalation by deflating the cuff and intermittently occluding the tracheal orifice. Alternatively, one-way speaking valves permit inhalation through the tube and exhalation through the larynx with the cuff deflated. A fenestrated, non-cuffed tube can also be used to facilitate this.

Care of Tracheostomy

The following are important points in the care of a tracheostomy:

1. Warmed humidified gases are used.

2. Fixation must be secure. A double tape is used, and this is changed at least once a day.

3. A dry dressing is used, changed 6-hourly or as frequently as needed. The wound is cleaned with a bactericidal solution.

4. Suctioning is carried out with a sterile suction catheter, using a sterile glove.

5. A chest X-ray is taken to confirm the position of the tip.

6. The tube is left in place for 7 days and thereafter changed every 4 days. Replacing the tube earlier than a week can be difficult as a tract may not have formed. If the tube needs to be changed earlier, or if it becomes dislodged, the stay sutures mentioned previously can be helpful. With the Shiley silastic tube or with the metal tubes, an inner tube can be changed frequently without replacing the main tube.

7. Frequent sputum and wound culture are taken.

8. Equipment must always be at the bedside to deal with an emergency. This should include the following:

(a) a new tracheostomy tube similar in size to the one in situ, plus another tube one size smaller;

(b) tracheal dilators, a nasal speculum and paediatric laryngoscope which may be used to dilate the stoma when replacing the tube;

(c) suction equipment and facilities for mechanical ventilation;

(d) resuscitator bag with facemask, laryngoscope and endotracheal tubes. If the tracheostomy tube cannot be reinserted, then orotracheal intubation should be carried out. It is often forgotten, in the heat of the moment, that the patient is able to be ventilated via the larynx.

Complications of Tracheostomy

The main complications can be classified as immediate, delayed or late.

1. *Immediate*

(a) Perioperative complications such as haemorrhage, surgical emphysema, pneumothorax, air embolism, and cricoid cartilage damage.

(b) Accidental disconnection.

(c) Misplacement in pretracheal tissues or right main bronchus.

(d) Compression of tube by cuff herniation.

(e) Occlusion of the tip against the carina or tracheal wall. This occurs if the tube used has an inappropriate length of shank or of the intratracheal portion.

2. *Delayed*

(a) Blockage with secretions. This may be sudden or gradual, but is rare with adequate humidification and suction.

(b) Infection of the tracheostome or the tracheo-bronchial tree.

(c) Distension of trachea with high-pressure cuffs, proceeding to ulceration and other sequelae.

(d) Mucosal alteration caused by the tip. This is due to asymmetrical inflation of the cuff.

(e) Deep erosion. This may lead to bleeding from the innominate artery or development of a tracheo-oesophageal fistula.

3. *Late*

(a) Granulomata of the trachea. These may cause respiratory difficulty when the tube is removed.

(b) Persistent sinus at tracheostomy site.

(c) Tracheomalacia and tracheal dilation.

(d) Tracheal stenosis. Some post-tracheostomy patients have radiological evidence of a small degree of narrowing which is more common at the cuff site than at stomal level. Stricture formation with severe obstruction usually occurs after several months and is commonly due to infection in the upper trachea. Treatment is by dilation or excision.

Decannulation

When the patient has been weaned from the ventilator, or when other indications for tracheostomy are no longer present, the tube can usually be removed, and the wound dressed and allowed to close spontaneously. Rarely, patients becomes emotionally "tied" to the tracheostomy, making decannulation difficult.

Management of the Obstructed Airway

The handling of the patient who has an obstructed airway is a delicate and often very difficult proposition. Specific management depends on the site, cause and severity of the obstruction.

Chapter 22: Mechanical Ventilatory Support

T. E. Oh

Respiratory support forms a major part of an Intensive Care workload, and is rarely required in isolation from other problems which may have their own adverse effects on respiratory function. There is a wide diversity of conditions leading to acute respiratory failure requiring mechanical ventilatory support. Some patients with acute lung disease can, however, be successfully treated without tracheal intubation and mechanical ventilatory support, using continuous positive airway pressure (CPAP) via a tight fitting anaesthetic face mask. Other accepted terms for mechanical ventilation include artificial, controlled, assisted, and intermittent positive pressure ventilation (IPPV), and continuous mechanical ventilation (CMV).

Indications

The classic indication for ventilatory support is reversible acute respiratory failure. Guidelines for instituting ventilation may be based on respiratory mechanics, oxygenation, and ventilation (Table 1). However, it is the trend of the values together with the clinical situation, which decides the need for intervention. Each respiratory variable must always be evaluated in the clinical context. If the clinical condition of the patient demands urgent ventilation, then complete assessment of the respiratory variables is unwarranted.

Ventilatory support is also indicated in certain serious disease states for the maintenance of adequate oxygenation and carbon dioxide elimination (Table 2).

Physiology of Mechanical Ventilation

Cardiovascular Changes

Mechanical ventilation is achieved by applying IPPV through an endotracheal tube. Compared with spontaneous ventilation, there is a reversal of pressure gradients with large pressures being applied. There is an increase in the mean intrathoracic pressure, with a resultant reduced venous return and fall in cardiac output. Left ventricular output is also decreased from a fall in right ventricular ouput, secondary to increased right ventricular

afterload (due to pulmonary microvascular compression during inspiration). If normal vascular reflexes are preserved, peripheral venous tone increases, restoring the venous gradient for return to the heart. This compensation fails when hypovolaemia exists, or when sympathetic responses are impaired.

The reduction in pulmonary blood flow leads to an increase in pulmonary vascular resistance which may be of importance when ventilating patients with lung disease. Adverse haemodynamic effects of IPPV may be minimized by maintaining an inspiratory:expiratory time ratio of less than 1, and by using rapid rates of inflation.

A less appreciated and unexpected effect of IPPV is an *increase* in left ventricular stroke volume during early inspiration. This is due in part to left ventricular compression by the raised intrathoracic pressure, and possibly also to reduced afterload from an increased pressure gradient between intra- and extrathoracic vascular beds. Thus cardiac performance in patients with severe left ventricular function may be improved by CMV, but this awaits further evaluation.

Lung Changes

IPPV results in some unfavourable pulmonary physiological effects, i.e. maldistribution of gas, progressive atelectasis with a reduced functional residual capacity (FRC), increased ventilation:perfusion (V/Q) mismatch, decreased compliance, and a reduction in surfactant. In spontaneous breathing, both ventilation and perfusion is preferentially distributed to the dependent zones of the lungs. With IPPV, however, preferential ventilation of the non-dependent regions occurs, resulting in increased (V/Q) mismatch. IPPV in the supine position also leads to decreased FRC, due in part to decreased lung volume from cephalad displacement by the diaphragm and abdominal contents. The loss of lung volume contributes to microatelectasis and decreased compliance. Decreased pulmonary hypoperfusion from IPPV, especially in the non-dependent regions, with maldistribution of gas, lead to increased alveolar dead space (increased dead space:tidal volume (V_D:V_T) ratio). Dead space ventilation increases with rapid rates, age, and lung pathology.

Venous admixture increases with IPPV because of multiple variables, i.e. increased V/Q mismatch, decreased FRC and progressive atelectasis. Periodic hyperinflation or "sighs" have been used to counteract atelectasis. However, the evidence for progressive atelectasis during IPPV is conflicting, and "sighing" is not now though to be important. Progressive atelectasis is less of a problem with larger tidal volumes, and surfactant recution may occur only with gross overdistention of alveoli. Venous admixture and the alveolar-arterial gradient (PAO_2-PaO_2 or A-aDO_2) has been shown to be reduced by using larger tidal volumes (i.e. 12 mL/kg), or by the addition of positive end expiratory pressure (PEEP).

Respiratory Alkalosis

Over-ventilation may produce moderate hypocarbia. Respiratory alkalosis decreases cardiac output, causes cerebral vasoconstriction, and increases haemoglobin affinity for oxygen (by causing a leftward shift of the oxygen dissociation curve). In addition, weaning from the ventilator may prove more difficult. Hypocarbia can corrected by the use of mechanical dead space.

Other Changes

Mechanical ventilation reduces the oxygen consumption required for respiratory work, which may vary from 2-3% at rest up to 40-50% in severe respiratory distress.

Antidiuretic hormone secretion is increased leading to water retention, and this is often accompanied by sodium retention as a result of the illness or surgery. Aldosterone secretion has also been reported to be increased by PEEP.

Assisted Ventilation

"Triggering" (or assist mode in North American terminology) is a system whereby the ventilator begins inspiration only after a spontaneous breath by the patient reduces airway pressure and initiates the ventilator cycle. The tidal volume is set by the intensivist and the patient determines the rate. For safety reasons, ventilators offer only an assist/control mode whereby the ventilator will deliver predetermined breaths if there is no spontaneous breathing by the patient. The theoretical advantage of "triggering" is to reduce inspiratory pressure and co-ordinate patient and ventilator. In practice, hyperventilation and patient exhaustion are commonly seen, and "triggering" is of little use other than to implement weaning or recovery from respiratory failure secondary to central depression.

Pressure support (assist) ventilation is a different entity to the above North American term for triggering. It is a technique which provides a constant preset airway pressure at the start of inspiration. Pressure support levels of 5-15 cm water (0.5-1.5 kPa) are usually used, which ceases after a given fraction of inspiratory time, or when inspiratory flow falls below a predetermined fraction of the initial inspiratory flow rate. Expiration is passive. The pressure support level is gradually decreased as the patient improves. Although there has been isolated case reports, consistent, clear clinical advantages over intermittent mandatory ventilation (below) or vice versa, have not been proven.

Intermittent Mandatory Ventilation

Intermittent mandatory ventilation (IMV) systems allow spontaneous breathing between the "mandatory" ventilator delivered breaths. The mandatory ventilation is further reduced by a reduction in ventilator frequency as the patient's ability to increase his own spontaneous minute volume improves. The spontaneous tidal volume is directly related to the patient's effort, whereas with "triggering", it remains a function of the ventilator. By allowing for some spontaneous breathing, IMV offers the following advantages:

1. There is a reduced need for sedation and muscle relaxants can be avoided.
2. A slower ventilator rate is possible thus allowing for potentially less barotrauma.
3. Venous return via the thoracic pump mechanism is augmented (by spontaneous breathing). Cardiac output is less depressed and higher levels of PEEP may be used when necessary.
4. The weaning process is facilitated, in part by the graduated exercising of respiratory muscles.

Synchronized IMV (SIMV) is a modification whereby the mechanical breaths are provided by triggered ventilation. If no breath is triggered within a predetermined time period, a mandatory ventilator breath is automatically delivered. There does not appear to be any clear cut clinical advantages of SIMV over IMV in critically ill patients.

Although IMV was originally introduced as a method to wean patients off controlled ventilation, it is now commonly used as an alternative to CMV. IMV may be instituted at the start, or after a 24-48 hour "rest period" of CMV. An initial minute volume of approximately 100 mL/kg with a rate of 8-10/min can be set, and the settings can be adjusted according to arterial blood gas measurements.

Mandatory Minute Volume

Mandatory minute volume ventilation (MMV) is another relatively new mode of mechanical ventilatory support. Essentially, the MMV system ensures that the patient always receives the same preset total (spontaneous and ventilator) minute volume. The spontaneous volume is measured by the ventilator which then contributes the remainder of the preset minute volume. In the early stages of ventilation, the patient's breathing is supported considerably by the ventilator. As the patient improves, his own spontaneous efforts contribute more to the minute volume, and ventilation by the machine automatically, gradually decreases. In contrast to IMV, progressive manual adjustments to the ventilator are unnecessary, i.e. the patient "self-weans". However, MMV circuits are relatively complicated. Spontaneous shallow, ineffective tidal volumes may not be differentiated by the ventilator, which would only sense the total spontaneous minute volume and thus inappropriately, contribute an inadequate mandatory volume. Its exact role in controlled ventilation still requires further evaluation.

Optimal Ventilatory Pattern

To offset the adverse haemodynamic and lung changes with IPPV and optimal ventilatory pattern can be:

1. A large tidal volume (10-15 mL/kg body weight) to minimize the increase in venous admixture (although dead space may increase in diseased lungs due to overinflation of more normal regions). Patients also tolerate large tidal volumes better than normal volumes of 7 mL/kg.

2. A relatively slow rate (10-12/min) to prevent large rises in V_D:V_T ratio.

3. An inspiratory:expiratory time (I:E) ratio of less than 1. Patients with obstructive airways, i.e. chronic obstructive airways disease or asthma may need smaller ratios, i.e. 1:3.

A *decelerating inspiratory waveform* has been suggested to lower airway resistance and improve gas distribution and oxygenation. *Accelerating flow* increases mean airway pressure and dead space. Nonetheless, clinical investigations on inspiratory waveforms are inconclusive, and waveform is not considered important provided the I:E ratio is kept below 1:1.

Inverse (or reverse) ratio ventilation uses a longer inspiratory (than expiratory) time. Advantages claimed are improvement in oxygenation and CO_2 elimination, from an effect of increasing FRC similar to that of PEEP. Disadvantages are also those seen with PEEP. This technique was first reported in children, but has since also been used in adults. I:E ratios of between 1.1:1 and 1.7:1 are deemed optional for oxygen delivery. Inverse ratio ventilation is commonly used with low levels of PEEP/CPAP, inspiratory hold, and low ventilation rates.

A *negative phase in expiration* (or *negative end expiratory pressure*) may help venous return to the heart but should preferably not be used. Most ventilated patients compensate adequately and volume deficit correction and/or inotropic agents are more important. Moreover, a negative expiratory phase may worsen ventilation: perfusion mismatch by encouraging airway closure at lung volumes near to FRC. *Expiratory flow retard* has been used to avoid premature airway collapse and air trapping in obstructive airways disease, but clinical usefulness is unproven.

As IPPV has physiological disadvantages, there has been increased use of ventilatory modes with a spontaneous breathing component (IMV or pressure support) or CPAP as alternatives to CMV, rather than as weaning techniques. Nevertheless, in the dangerously hypoxic patient, IPPV remains the mainstay management.

PEEP

More favourable distribution of inspired gas occurs with the use of PEEP. In general, PEEP is indicated when an adequate fractional inspired oxygen concentration (FIO_2) fails to maintain satisfactory oxygenation (i.e. PaO_2 60 mmHg or 8 kPa or less). PEEP is used by some "prophylactically" during controlled ventilation (as it will nearly always improve oxygenation), but there is no evidence that "prophylactic" PEEP alters the course of the acute lung disease. PEEP improves oxygenation probably by reducing terminal airway closure and increasing FRC leading to a reduction in $A\text{-}aDO_2$.

The usual range employed is 5-15 cm of water (0.5-1.5 kPa) but higher values have been used. With the use of higher pressures, the fall in cardiac output caused by the raised intrathoracic pressure may counteract the beneficial effects of PEEP on oxygenation. Optimal levels of PEEP can be found with the use of pulmonary capillary wedge pressure (PCWP), cardiac output, and mixed venous oxygenation tension measurements, and with appropriate use of inotropic agents. However, PCWP readings in the presence of PEEP need to be interpreted with caution. When CVP and PCWP measurements are not available, lung compliance and the clinical indices of cardiac output may be used to derive an optimal PEEP level. PEEP may be applied with IMV to lessen the decrease in cardiac output. Higher levels of PEEP may then be introduced but the increased attendant risk of barotrauma.

In a few patients PEEP may worsen PaO_2, though to be due to extensive redistribution of pulmonary blood flow to non-ventilated regions of the lung, thus increasing the shunt fraction. Other adverse effects of PEEP include reduced renal blood flow, raised intracranial pressure, and an increased risk of barotrauma. PEEP is further discussed in Chapter 25, Acute Respiratory Distress Syndrome.

CPAP

Since PEEP is a residual airway pressure above atmospheric at the end of expiration, it can be used during spontaneous or mechanical ventilation. With spontaneous PEEP (SPEEP), the airway pressure becomes less positive during inspiration, and eventually negative at the height of inspiration. CPAP may also be used during spontaneous ventilation. It is *continuous* positive airway pressure, with positive airway pressure maintained *throughout* the whole respiratory cycle. CPAP need not be confined to spontaneous breathing. It may be used with IMV, becoming effective during the spontaneous breathing phase.

The physiologic lung effects and disadvantages of CPAP are similar to PEEP, CPAP or SPEEP is provided by differences in circuit design. Attention to circuit resistances and expiratory valves of ventilators are extremely important, as work of breathing may be markedly increased. Work of breathing is least when positive airway pressure is constant, i.e. less with CPAP than SPEEP.

CPEEP/SPEEP may be applied via a face mask, endotracheal or tracheostomy tube, and specially designed nasal prongs or nasal mask. Tight-fitting face mask CPAP/SPEEP offer an alternative to intubation in certain selected patients in respiratory failure, but facial skin pressure lesions and aspiration risks are disadvantage. The risk of aspiration may be reduced with concomitant use of a nasogastric tube to prevent gastric distension. Nasal devices are better tolerated and safer than face masks, but mout breathing tolerated and safer than face masks, but mouth breathing reduces effectiveness. They are used in children and for managing obstructive sleep apnoea. In general, CPAP/SPEEP may be used in spontaneously breathing patients in acute respiratory failure, and during weaning.

Management of Mechanical Ventilatory Support

Nursing Care and Observations

Nursing care is vitally important in patients receiving mechanical ventilatory support. When ventilation is controlled completely with sedation and paralysis, the nursing care will be the same as that of an unconscious patient. Additional observations, however, need to be made and recorded. The patient's colour, chest movements, air entry to both sides, and synchronization with the ventilator should be observed frequently between regular recordings of vital signs. Recordings of inflation pressure, frequency, expired minute volume or tidal volume, FIO_2, and inspired gas temperature should be carried out every hour. Tube intracuff pressure should be checked every time the cuff is inflated. Circuit leaks must be detected and the ventilator alarm systems should not be switched off. Patient communication is important. A ventilated patient must always be spoken to as if he were fully awake and alert. A brief explanation should be given prior to any procedure being performed.

Patients on life-support such as a ventilator should never be left unattended, because failure of the system or development of life-threatening complications (i.e. pneumothorax) may occur. Hence the nurse must be alert to any sudden changes in system performance, or any acute development of patient distress, cyanosis, tachycardia, increased inflation pressure, and unequal air entry.

Clearance of Secretions

Endotracheal suction is a very important aspect of the care of intubated patients. It should be performed with a sterile glove technique. The catheter is introduced gently into the trachea, and intermittent suction is applied as the catheter is slowly rotated and with drawn. This procedure should be limited to 15 seconds. Manual hyperinflation of the lungs with 100% oxygen should be done for 2-3 minutes before and after suction. The use of PEEP in this pre-oxygenation inflations may improve oxygenation and minimize suction desaturation in hypoxic patients with decreased FRC. If PEEP or CPAP is already being applied, a self-sealing endotracheal tube adaptor should be used with tracheal suctionings. Severe oxygen desaturation may otherwise occur on disconnection from the ventilator (when positive airway pressure is lost). Vibration or percussion of the chest during lung deflation from a hyperinflated position helps to loosen secretions so that they may be removed by suction. Aspirated sputum should be sent for microbiologic culture and sensitivity tests.

Sedation

Sedative and muscle relaxant drugs are given to the patient to enable synchronization with the ventilator. "Fighting" the ventilator leads to uncoordinated ventilation, increased oxygen consumption, and increased risk of complications from the endotracheal tube (i.e. accidental extubation, and laryngeal damage). The drugs used include midazolam, opioids, alcuronium, and pancuronium. Requirements vary from patient to patient, but inadequate sedatio or oversedation are to be avoided. A continuous infusion of a sedative is preferable to intermittent IV injections. Requirements for sedation are lessened with the use of spontaneous breathing modes.

Monitoring of Ventilatory Therapy

1. *Arterial Blood Gas*

Serial arterial blood gas (ABG) estimations are the most direct and accurate means of assessing adequate oxygenation and carbon dioxide elimination. Any adjustment or change of ventilatory parameter (i.e. FIO_2, minute volume, or mechanical dead space) should be assessed 20-30 minutes later by an ABG analysis. The effect of altering PEEP on gas exchange could be assessed earlier, as FRC and PaO_2 changes probably occur within one to two minutes after a change in PEEP. Although nomograms are available for the required dead space to achieve normocarbia they are unreliable in clinical practice. Dead space increments of 50-100 mL should be checked by ABG analysis so that the desired $PaCO_2$ level can be attained.

2. *Pulse Oximetry*

Continuous oxygen saturation monitoring by non-invasive pulse oximeters are recommended for severely hypoxic and haemodynamically unstable patients. Adjustments or changes of ventilatory parameters and modes can be made with oxygenation responses observed almost immediately. Pulse oximetry is more practical and commonly used than invasive continuous mixed venous oxygen saturation.

3. *End-Tidal CO_2*

Continuous monitoring of end-tidal expired CO_2 using a CO_2 analyzer is useful in certain situations, i.e. therapeutic hyperventilation, but is not routinely necessary.

4. *Lung Function Tests*

Assessment of ventilation: perfusion mismatch can be performed regularly by measuring A-aDO_2 and the V_D:V_T ratio. Tests of ventilatory capacity may be indicated in some patients, but tests of lung mechanics are generally not practical.

5. *Serial Chest X-Rays*

Weaning

An aim of ventilatory therapy is to wean off mechanical ventilatory support as soon as practicable. On the other hand, weaning should not be attempted before the patient has recovered sufficiently to regain adequate ventilatory and pulmonary reserves. Guidelines for weaning are essentially the converse of values used for instituting controlled ventilation. In general, weaning will not be successful if there is an accompanying major organ failure, or if the patient still requires a high FIO_2 to maintain adequate oxygenation. Nevertheless, the decision to initiate the weaning process is often subjective as traditional criteria can be unreliable. Weaning can be initiated without having to discontinue PEEP first, as was previously recommended.

Weaning is traditionally accomplished with a T-piece system, using adequate humidification and oxygen concentration. The use of PEEP can be replaced with CPAP using the appropriate CPAP valve and circuit. There must be no residual effects of sedatives or muscle relaxants. Vital signs, ABGs and respiratory variables should be monitored closely during the weaning process. The CPAP is gradually decreased in line with satisfactory PaO_2 results. Periods of spontaneous ventilation are gradually lengthened until mechanical ventilatory support is required only at night. The patient is then taken off the ventilator at night after at least 2 consecutive days of spontaneous breathing. Removal of the tracheostomy tube may be carried out after another 2-3 days. If secretions are troublesome, replacement with a smaller tube or a fenestrated tube enables removal of secretions and allows the patient to breath more easily.

The use of IMV and/or pressure support in weaning avoids the drastic change from CMV to spontaneous breathing via a T-piece. Ventilator delivered breathing is progressively reduced as the patient's respiratory function improves. The patient is then weaned to spontaneous breathing by a T-piece or CPAP when IMV ventilator breaths are as low as 3-4/min or pressure support required is less than 3 cm water (0.3 kPa). IMV and/or pressure support may be useful in patients who are difficult to wean off CMV (i.e. chronic bronchitis and those with prolonged ventilatory support). Weaning time may be shortened in these patients.

Other Methods of Ventilation and Gas Exchange

High Frequency Ventilation

"High frequency ventilation" is a confusing term which does not refer to a single homogenous entity. Three main basic techniques can be identified.

1. *High Frequency Positive Pressure Ventilation (HFPPV)*

HFPPV delivers humidified gas through an insufflation catheter, bronchoscope, or cuffed endotracheal tube, at a preferred rate of 1-2 Hz (60-120/min). Adequate alveolar ventilation and arterial oxygen can be achieved with a reduction of peak airway pressure (and circulatory interference), and an improvement in pulmonary gas distribution. It has been successfully used during laryngoscopy and bronchoscopy, and in adult and neonatal intensive care. The performance of HFPPV may be specific to the device, as reported features refer to a device of small internal volume and static compliance.

2. *High Frequency Jet Ventilation (HFJV)*

This is probably the most widely used form of HFV used today. HFJV delivers dry gas under a high pressure (about 50/lbsq inch or 345 kPa) at rates of 2-10 Hz (120-600/min), by means of fluidic solenoid, or rotating valve flow controllers. Driving pressure, frequency and I:E ratio are usually adjustable. Gas entrainment in the proximal airway is common but not invariable. Expiration is passive and PEEP may be added. Humidification depends on entrainment of additional humidified gas through a side arm, placing a humidifier before or after the cycling device, or a saline drip into the circuit, immediately in front of the jet nozzle. The optimal positioning of the jet nozzle within the trachea is unknown. Gas exchange occurs by ordinary convective gas transport, possibly enhanced by some turubulent mixing generated by the jet, as tidal volumes are extremely small at 1.0-2.5 mL/kg. Although peak airway pressure is reduced, barotrauma has occurred, since exhalation is dependent on passive lung and chest wall recoil driving gas out of the endotracheal tube. HFJV has been successfully used to treat bronchopleural or tracheal disruption, bronchopleural fistula, ventilator weaning and emergency percutaneous trans-tracheal ventilation. It has been associated in neonates with tracheal injury and obstruction due to inadequate humidification.

3. *High Frequency Oscillation (HFO)*

HFO used a piston, loudspeaker or similar device to oscillate at 3-20 Hz (180-1200/min), and drive a very small volume of gas into the airway and suck an equal volume back out. A steady fresh gas (bias) flow at the top of the endotracheal tube provides oxygen and removes carbon dioxide. Alveolar gas exchange is postulated to be due to facilitated diffusion. A higher mean airway pressure can be achieved, but less than peak airway pressure by conventional means. Ventilation-perfusion inequalities may be minimized. HFO currently remains more of a research rather than clinical technique.

4. *Combined High Frequency Ventilation (CHFV)*

A combination of CMV (usually at slower rates) with a HFV technique, either between or superimposed upon CMV breaths is possible. There have been isolated reports of CHFV, but this hybrid mode has yet to be clinically evaluated in full.

The role of high frequency techniques in Intensive Care awaits further evaluation. Many issues such as humidification, optimal characteristics and technical device flaws still remain unresolved. Variations of a technique may be adapted to different clinical situations. However, high frequency ventilation has not been shown to offer major advantages over conventional modes of ventilation.

Independent Lung Ventilation

Independent lung ventilation (ILV) is achieved by using a double lumen endobronchial tube to ventilate each lung separately. Plastic double lumen tube ("Broncho-cath", National Catheter Co) are preferred to more irritant traditional rubber Carlens or Robert-Shaw tubes. Two ventilators are usually required and settings and ventilatory modes can be selectively applied without need for synchronization. ILV is an acceptable form of ventilatory support in respiratory failure with a unilateral or different lung pathology such as unilateral oedema, aspiration, or chest trauma.

Extracorporeal Membrane Oxygenation (ECMO)

Controlled trials have shown no benefits of ECMO over conventional ventilation. A modified technique of extracorporeal CO_2 removal with low frequency IPPV and PEEP has been reported to produce good results in critically ill severely hypoxic patients. Cost, logistical and technical difficulties limit use of EMO in Intensive Care.

Chapter 23: Ventilators

T. E. Oh

Ventilators are devices used for mechanical ventilation. In Intensive Care, negative pressure ventilators such as the cuirass and iron lungs, are not useful and are not discussed. Instead, intermittent positive pressure ventilation (IPPV) is accomplished with positive pressure machines.

Ideal Requirements

There are numerous ventilators available today, each with different working principles, behaviour, and special functions. For use in an ICU, an ideal ventilator should provide for:

1. Ability to ventilate all sizes of patients, from neonates to adults. However, neonatal ventilators have evolved from T-piece, continuous flow occlusion systgems, because of size constraints imposed by their patients. While these systems are simple and have low resistance and dead space, precise control of respiratory patterns and monitoring of gas volumes are

difficult. Modern ventilators catering for older children and adults are more complex but offer greater versatility.

2. Versatility of operation, i.e. ability to produce optimal patterns of ventilation for each clinical situation by variation of mode and parameters such as inflating pressure, tidal volume, rate, inspiratory:expiratory (I:E) ratio.

3. Delivery of accurate, pre-determined, stable oxygen concentrations from 21-100%.

4. Complete delivery of all preset volumes despite changes in patient lung characteristics.

5. Minimal circuit resistance and impedance to allow spontaneous breathing modes without incurring excessive work of breathing.

6. Effective and safe humidification of gases and nebulization of bronchodilator drugs.

7. Monitoring of respiratory variables and alarm facilities. These two requirements are complementary in modern ventilators, i.e. reliable and sensitive disconnect alarms relate to continuous monitoring of airway pressure and expired volume.

8. Application of positive end expiratory pressure (PEEP) and continuous positive airway pressure (CPAP).

9. Adequate safeguards (cross-)infection, such as simplicity of sterilization (i.e. using an autoclavable patient circuit).

10. Electrical and gas safety features including continuing function in the event of an electrical or gas source failure, or high pressure relief valves to prevent barotrauma.

11. Simplicity of use and maintenance, reliability and robustness.

Driving Mechanism

All ventilators require a power source or driving mechanism. The driving mechanism may deliver the gas to the patient directly (single circuit), or by way of another mechanism (double circuit), i.e. ventilator compression of a bag or bellows, which in turn delvers the gas to the patient. The types of driving mechanisms used in ventilator may be:

1. *Electrical motors* which may drive either:

(a) an air compressor, with the gas pressure produced being used to ventilate the patient; or

(b) a piston, with the piston drive mechanism being rotary- or linear-drive.

2. *Pneumatic* which may be further subdivided into:

(a) high pressure, utilizing wall source air or oxygen; or

(b) low pressure, with wall source gas passing through a reducing valve or a venturi injector.

3. *Spring tension* driving a bar or bellows which then delivers the gas.

4. *Weight* on bellows, i.e. mass utilized as a generating pressure source.

Control Mechanism

Every ventilator demonstrates four phases: inspiratory, inspiratory to expiratory (I to E) cycling, expiratory, and E to I cycling. The control mechanism which initiates each phase of ventilation may operate mechanically, electronically, via fluidic components, by microprocessors, or by any mixture of these. Microcomputers are being increasingly used by new ventilators to control complex electronic valves and regulators, often using servo-controlled (feedback) flow mechanisms.

Paned controls for ventilatory parameters vary from ventilator to ventilator. Gas volumes can be preset by direct control of any two of the three parameters of inspired minute volume, tidal volume and respiratory rate. Duration of inspiration and expiration can be set by any of the following controls:

1. Direct control of rate with a fixed I:E ratio (i.e. 1:2).

2. Direct rate control with variation of I:E ratio by altering the inspiratory time. This is accomplished by tidal volume and flow (i.e. volume per unit time) changes. High flows with small tidal volumes will decrease inspiratory time and decrease the I:E ratio.

3. Direct control of inspiratory time (which may also include control of pause time) or both inspiratory and expiratory times by timing mechanisms.

Cycling

Some ventilators use the same mechanism to initiate both inspiration and expiration, but others use one mode of cycling to end inspiration and another to end expiration.

1. Inspiratory to Expiratory Cycling

Inspiration can be terminated by the following modes:

(a) *Time cycling.* Cycling is controlled by a timing mechanism.

(b) *Pressure cycling.* Cycling occurs when airway pressure reaches a pre-determined value.

(c) *Volume cycling.* Expiration is started after a fixed tidal volume has been delivered. Some ventilators which are time or pressure cycled use a double circuit "bellows in bottle" delivery system, with the tidal volume being set by limiting the bellows travel. If the inflating pressure or cycling pressure in these machines is set by very high (relative to airway pressure), then the preset tidal volume will always be delivered. Hence, these machines when used in this manner are strictly speaking, volume limited, time or pressure cycled, but may also be referred to as being volume cycled.

(d) *Flow cycling.* Inspiration is terminated when gas flow to the patient falls to a critical preset value. It is an uncommonly used mechanism.

(e) *Mixed cycling.* More than one mode of cycling is possible because of independent cycling mechanisms, or variable performance of a single mechanism.

2. Expiratory to Inspiratory Cycling

Triggering (Assist)

Expiratory to inspiratory cycling may use any of the methods terminating inspiration. In addition, there is patient cycling, in which the patient starts to inhale and in doing so, initiates inspiration. This is also called triggering, and the cycling mechanism depends on the slight negative pressure or gas flow generated by the patient. The sensitivity of the triggering mechanism can vary, and there is always a slight delay between sensing the inspiratory attempt and initiating inspiration. Patient triggering is thus usually unsatisfactory at high respiratory rates. Patient cycling also decreases the expiratory time, and hence the I:E ratio rises from the set value.

Triggering is known in North America as the "assist" mode, and a patient-cycled machine can be referred to as an assister. (A ventilator which controls inspiration by time cycling is called a controller.) An assist/control mode then allows triggering, but which also initiates mechanical ventilation if spontaneous respiration ceases. Most ventilators allow assist/control, as assist-only machines are hazardous if the patient fails to take spontaneous breaths.

Classification

Classification of ventilators facilitates the understanding of their functional characteristics. The intensivist can then choose the most appropriate ventilator for his needs, use that ventilator optimally, and predict the effect of lung changes on ventilator function. Classification which have been described include:

1. Volume or Pressure Preset (Hunter 1961)

Volume preset machines can be set to deliver a fixed tidal volume, and do so despite changes in lung characteristics. Increase in airway resistance or decrease in compliance will result in an increased airway pressure. Any leaks in the circuit will be uncompensated and will result in a fall in inspired minute volume.

Pressure preset machines generate a preset pressure, and I to E cycling occurs when a predetermined airway pressure is reached. Reduced compliance or increased airway resistance will usually result in a fall in minute volume (measured as expired volume). Small leaks in the circuit will, however, be compensated for, because the pattern of airway pressure remains unchanged. In general, pressure preset ventilators are not useful in the ICU. This classification, although simple and useful is no longer adequate.

2. Force Generators (Norlander 1964)

Ventilators are classified based on a concept of force, assesed as a product of flow and pressure, using a test lung. Two major groups are *constant force generators* (subdivided into those with adjustable or non-adjustable flow) and *increasing force generators* (subdivided into those with direct or indirect action). This classification is not useful. Cycling and some decreasing force generators are ignored.

3. Stable or Flexible Volume and Flow (Grogono 1972)

Minute volume, tidal volume, and inspiratory volume flow are classified as *"stable"* if constant values are maintained, and as *"flexible"* if the values change with changes in the patient's lungs (Table 1). However, "stable" characteristics in normal patients may become "flexible" with grossly abnormal lungs, and modes of cycling are not classified.

4. Flow Pattern, Force and Cycling (Baker 1974)

Ventilators are considered as flow producers (Table 2). *Flow-controlled* (or load-independent) ventilators can maintain a predetermined inspiratory flow pattern against patient impedance. *Flow-uncontrolled* (or load-dependent) machines cannot maintain the flow pattern; i.e. flow is affected by patient lung changes. In general, flow control is more likely to be achieved by a high driving force or generating pressure. An arbitrary generating force of 50 mmHg (6.7 kPa) was chosen to divide flow-controlled from flow-uncontrolled.

Other characteristics are grouped into force patterns (*constant, varying* and *adjustable*) which in turn, are subdivided into their methods of *I to E cycling.*

The division into flow-controlled or uncontrolled is dependent upon the generating pressure. Since a high value was selected, this classification is more suited to abnormal lung mechanics. Nonetheless, this classification is useful to predict how a ventilator will perform in a clinical setting, but unfortunately, it is not commonly used.

5. Flow or Pressure Generator (Mapleson 1969)

This widely used classification considers inspiratory and expiratory flow with their methods of cycling, although clinical usefulness involves mainly inspiratory flow and I to E cycling (Table 3). A *flow generator* is a ventilator with a high generating pressure, producing an inspiratory flow which is unaffected by patient lung changes. The flow pattern of a flow generator may be constant or non-constant (i.e. sine wave flow pattern produced by a rotary-drive piston).

A *pressure generator* has a lower generating pressure to produce an inspiratory flow which can be influenced by changes in lung characteristics. Although the flow pattern may vary, the pressure wave form remains the same, and may be either constant or non-constant (i.e. increasing or decreasing pressure generators). Both flow and pressure generators are subdivided into methods of cycling.

Although this classification divides ventilators according to the generating pressure produced to drive gas into the lungs, it is actually a spectrum, with transition from one group to the other at some intermediate point. A ventilator behaves like a flow generator when the generating pressure is high enough to disregard patient impedance. A pressure generator may become a flow generator if its generating pressure is increased to exceed alveolar pressure by 10 times. Some ventilators allow control of generating pressure, and these machines may then be used either as flow generators or pressure generators.

6. Ventilator Evaluation Data Forms (Desautels 1985)

Forms are completed on ventilators, giving details such as power and drive mechanisms, modes, waveforms, specifications, options, controls, and ease of use. These forms compare ventilators objectively, and when used with bench-test evaluation and Mapleson's classification, give comprehensive information for clinical use.

7. High Frequency Ventilation

The above classification systems are not applicable to high frequency ventilators. Types or techniques of high frequency ventilation are discussed in Chapter 22, Mechanical Ventilatory Support, but are, as yet, to be classified in a clinically useful system.

Minute Volume Dividers

A few ventilators, in addition to being classified into any of the above classifications, can be grouped as *minute volume dividers* or *"flow choppers"*. The minute volume of gas is preset from the flow meters of the gas source. The tidal volume and inflation pressure are determined, thus deriving the rate. No increase in minute volume can be achieved by the patient, even by triggering the ventilator.

Ventilatory Modes or Special Features (See Chapter 22)

1. Controlled Mechanical Ventilation (CMV)

Modern ventilators are able to perform as volume-limited, time cycled flow generators, delivering preset tidal volumes and rates.

2. Patient Triggering (Assist/Control) (See above)

3. Intermittent Mandatory Ventilation (IMV)

IMV aids weaning by obliging the patient to breathe spontaneously via a one-way valve, in between the mandatory ventilatory cycles. A modified IMV circuit may result in

hyperinflation when a mandatory breath is "stacked" on top of a spontaneous one. This is overcome in some new ventilators by provision of a synchronized facility, i.e. SIMV.

4. Pressure Support or Assist

This is not to be confused with triggering. Pressure support/assist is a mode whereby the patient initiates inspiration and the ventilator delivers a breath up to a constant preset positive airway pressure. As weaning progresses, the pressure support level is decreased stepwise.

5. Mandatory Minute Volume (MMV)

MMV ventilation aids weaning. It incorporates a modified circuit so as to deliver a mandatory preset minute volume which is the sum of spontaneous respiration and mechanical ventilation. The patient breathes spontaneously and the ventilator makes up for the deficit in the minute volume, i.e. mechanical ventilation varies minute by minute, inversely to spontaneous respiration.

6. Positive End Expiratory Pressure (PEEP)

PEEP is provided by incorporating an expiratory resistance in the breathing circuit. This can be achieved with a constriction, a spring-loaded valve, a weighted valve, an under-water column, a venturi valve, an electronically controlled scissor valve, or a pressure-actuated solenoid valve placed in the expiratory part of the circuit. All devices produce some retardation of expiratory flow before the final pressure is reached, with a resultant increase in mean airway pressure. Devices which offer gas flow resistance at an orifice are "flow resistors" and those which are "cap" valves opening at a preset pressure are "threshold resistors". A threshold resistor valve presents minimal resistance to gas flow above its threshold (opening) pressures, and unlike flow resistors, pressure gradient across the valve is independent of the gas flow. The lower resistance of threshold resistors are advantageous in reducing work of breathing and avoiding excessively high airway pressures from coughing and straining. PEEP is discussed further in Chapter 22.

7. Continuous Positive Airway Pressure (CPAP)

CPAP or constant positive-pressure breathing allows spontaneous respiration at an elevated baseline pressure when the ventilator is used in the assist mode. The objectives are similar to PEEP.

8. Expiratory Flow Retard

Expiratory retard is accomplished by a restriction on the expiratory outflow tract. The airway pressure gradient across the restriction is proportional to the gas flow through it, and decreases as flow decreases in expiration. Hence airway pressure drops slowly to atmospheric when expiratory gas flow ceases, whereas in PEEP, pressure is held at a value above atmospheric when flow ceases. However, if the expiratory time is insufficient to allow full expiration in between ventilator breaths, expiratory retard will result in PEEP. In either case, the objective of expiratory retard is to maintain a positive airway pressure to prevent airway

closure in chronic obstructive airways disorders, and to favour lung emptying in such patients. However, expiratory retard involves the risks of hyperinflation and circulatory depression.

9. End Inspiratory Plateau (EIP)

End inspiratory plateau (or pause, or hold) includes pressure hold and volume hold. With pressure hold, a preset pressure is reached and held for a period of time. EIP may be regarded as a prolongation of the inspiratory phase. EIP may improve ventilation-perfusion mismatch by decreasing the physiological dead space: tidal volume ratio (V_D:V_T). However, the effect is small and EIP may worsen circulatory depression. The benefits of EIP remain largely theoretical.

10. I:E Ratios

Many ventilators do not offer control over the I:E ratio, but this is a desirable feature. Inverse ratio ventilation is an alterantive method to increase FRC.

11. Negative End Expiratory Pressure (NEEP)

The principle of NEEP is to counteract the increased intrathoracic pressure caused by IPPV. However, most ventilated patients compensate adequately, and volume deficit correction and/or inotropic agents are more important. Moreover NEEP may worsen ventilation:perfusion mismatch when airway closure occurs at lung volumes near to the functionals residual capacity. NEEP is usually achieved with a venturi to entrain circuit gas.

12. Sighs

Sighs are programmed periodic hyperinflations. The objective is to prevent progressive atelectasis, but sighs are poorly tolerated by patients, and are probably not necessary with the use of large tidal volumes.

Clinical Considerations

When using a ventilator, the important considerations are:

1. The length of the inspiratory phase.
2. The mode of I to E cycling.
3. Whether cycling is affected by changes in patient lung characteristics thus altering the tidal volume.
4. The length of the expiratory phase, which should be adequate to allow expiration of the inspired tidal volume.
5. Whether E to I cycling is affected by lung changes.
6. The modes of ventilation available.
7. The resistance of components for spontaneous breathing such as demand valves.

Although accelerating and decelerating flow patterns have been advocated, there is no evidence to suggest that any particular wave form is superior in efficient ventilation. Constant

flow generators produce a square flow wave form whereas constant pressure generators produce a downward tapering flow wave form.

In general, ventilators which can deliver gas volumes unaffected by any change in the patient's lungs are preferred in the ICU. Classification shows these ventilators to be:

1. Flow generators, which are either time or volume cycled, using Mapleson's classification.

2. Flow-controlled (Load-independent), constant or nonconstant force, which are either time or volume cycled, using Baker's classification.

3. Volume preset, using Hunter's classification.

The working principles of a ventilator being used should be understood to enable it to be classified. The panel controls should be familiarized in order to correctly set tidal volume, rate, inspiratory time, and the alarm mechanisms, Oxygen concentration can be set directly or via an attached oxygen blender. Humidifiers are discussed in Chapter 24, Humidification. Bacterial contamination of ventilator and patient can be minimized by circuit design, protocols for circuit changes, and the use of bacterial filters.

Correct performance of the ventilator is assessed by observation of patient chest movements, chest auscultation, and monitoring respiratory variables. The inspired tidal volume may be less than the preset value because of gas compression within the circuit. The volume of gas compressed is directly related to the end inspiratory pressure. This internal compliance is approximately 3 mL/cm water (0.03 L/kPa). Hence expired volumes should always be measured (i.e. with a Wright's respirometer).

Detailed descriptions of individual ventilators are provided elsewhere.

Portable Ventilators

Portable ventilators facilitate transport of ventilated critically ill patients. Resuscitators may be used for short-term patient transport. These are manual self-inflating bags, manual oxygen-inflating bags, or oxygen powered resuscitators. Portable ventilators are specifically designed ventilators for patient transport. The Drager Oxylog and Ohmeda Logic 07 are such compact portable ventilators.

They are oxygen powered with a fluid logic controlled circuit. Air entrainment is possible, thus allowing either 50-60% oxygen or 100% oxygen to be used. The I:E ratio is fixed. IMV and PEEP (using an AMBU or Boehringer valve) modifications are also possible.

Chapter 24: Humidification

T. E. Oh

The upper airway normally warms, moistens and filters inspired gas. When these functions are impaired by disease factors, or when the naso-oropharynx is bypassed by endotracheal intubation, artificial humidification of inspired gases must be provided.

Physical Principles

Humidity is the amount of water vapour in a gaseous environment. The two measures of humidity are:

1. *Absolute Humidity (AH)*

This is the total mass of water in a given volume of gas at a given temperature (g/m^3).

2. *Relative Humidity (RH)*

This is the ratio, expressed as a percentage, of the mass of water in a given volume of gas to the mass of water required to saturate the same volume of gas, at a given temperature.

The mass of water contained in a unit volume of gas when fully saturated exerts a saturated vapour pressure (SVP). SVP is proportional to temperature and this relationship is exponential (Table 1). Hence the addition of further water vapour to the gas can only occur with a rise in temperature.

Physiology

The respiratory tract from the nose to terminal bronchioles is lined with columnar mucus-secreting epithelium. Inspired gas is warmed and humidified in the naso-oropharynx and reaches the upper trachea with a RH of about 90% and a temperature of 32-36 °C. Humidification and warming continue down the airways so that alveolar gas is fully saturated at 37 °C (i.e. AH or water content of 43 g/m^3). Normal breathing through the nose adds about 75% of the total water content before the inspired gas reaches the larynx, whereas with mouth-breathing, inspired gas is only about 25% saturated above the pharynx.

Heat is required to warm the inspired gas to 37 °C and to provide for the latent heat of vaporization of water. A normal man under resting conditions loses approximately 250 mL of water and 1.5 kJ (350 kcal) per day from the respiratory tract. A proportion of heat and water (10-25%) is returned to the mucosa of the upper respiratory tract on expiration, i.e. there is a condenser effect which conserves heat and water.

Watery mucus coating the tracheobronchial mucosa is moved towards the glottis, along with solid particles, by cilia (at a rate of 10 mm/min at 37 °C and 100% RH). Ciliary activity

ceases at temperatures above 41 °C, and slows down when RH falls below 75% at 37 °C (AH of 32 g/m^3). Temperature appears to be unimportant if RH is between 75% and 100%.

The humidifying functions of the airway above the trachea can be impaired by many factors including cold, dry inspired gases, upper respiratory tract infection (URTI), dehydration and hyperventilation.

Clinical Applications of Humidification

1. Tracheal Intubation

The need for humidification of intubated and recently tracheostomized patients in the ICU is unquestioned. The naso-oropharynx is bypassed and the inspired gas RH falls to 50% or less. This presentation of cold, dry gases to the trachea and bronchi has adverse effects such as:

(a) Increased mucus viscosity with crusting, inspissation, tracheal inflammation, and even frank mucosal ulceration.

(b) Depressed ciliary function.

(c) Microatelectasis from obstruction of small airways.

(d) Airways obstruction due to tenacious or inspissated sputum.

The inspired gases should be delivered to the endotracheal tube or tracheostomy close to saturation at body temperature (i.e. a minimum RH of 75% when warmed to 37 °C).

It has been shown that humidification of anaesthetic gases reduces postoperative pulmonary complications and prevents undue falls in body temperature during surgery.

Humidification in an ambulant patient with a permanent tracheostomy presents many practical problems. Fortunately in such a patient, continuous humidification is unnecessary as metaplasia of the tracheal epithelium occurs, so that eventually the trachea is able to humidify the inspired gas. Nevertheless, humidification may be indicated during an acute respiratory infection.

2. Rewarming

The respiratory tract is an important avenue by which body temperature can intentionally be adjusted by heat exchange. The heat content of saturated gases may be used as a central warming device in the treatment of hypothermia.

3. Drug Delivery

Drugs may be delivered to the respiratory mucosa via micro-droplets of water (aerosols) in the inspired gas. Aerosol therapy is commonly used to administer

bronchodilators. The distribution and deposition of aerosol determine the effectiveness of endobronchial drug application. Aerosol drug delivery should be aimed at the lower respiratory tract. Most of the drug deposited in the upper respiratory tract will be removed with secretions, with only a small proportion absorbed.

4. Acute Upper Respiratory Tract Infection (URTI)

The aim of humidification therapy in URTI is to thin and prevent desiccation of secretions. It is unclear whether the deposition of water micro-droplets on inflamed mucosal membranes is beneficial. Aerosol therapy is provided for adults and older children via masks using high flows and saturation at body temperature. Small children with URTI are generally managed in mist tents.

5. Lower Respiratory Tract Disease

Aerosol therapy has been used in lower respiratory tract diseases such as cystic fibrosis, emphysema and chronic bronchitis, in conjunction with other supportive measures (i.e. physiotherapy, mucolytic agents, bronchodilators, and intermittent positive pressure breathing by mask). The use of humidification to prevent secretion desiccation during an acute illness in these patients is useful, but the true benefits of long-term aerosol therapy, although theoretically sound, are largely unproven.

Ideal Humidification

The basic requirements of a humidifier should include the following features.

1. The inspired gas is delivered into the trachea at 32-36 °C and with a water content of 33-43 g/m^3.

2. The set temperature remains constant and does not fluctuate.

3. Humidification and temperature is unaffected by large ranges of fresh gas flow - especially high flows.

4. The device is simple to use and to service.

5. Humidification can be provided for air, oxygen or any mixture of inspired gas (including anaesthetic agents).

6. The humidifier can be used with spontaneous or controlled ventilation.

7. There are safety mechanisms (with alarm) against overheating, overhydration, and electrocution.

8. The resistance, compliance, and dead space characteristics do not adversely affect spontaneous breathing modes.

9. The sterility of the inspired gas is not compromised.

Methods and Devices

1. Saline Drip

Direct instillation of water or saline by continuous drip has no place in the ICU (with the exception of short-term use in high frequency jet ventilation). This method is inefficient and may cause loss of alveolar surfactant similar to that from excessive bronchial lavage. The risks of drowning are substantial.

2. Condensers

A condenser performs the function of the nasopharynx by retaining heat and moisture from expired gas through condensation, and returning them to the inspired gas which passes over the condensate. Heat and moisture exchanger (HME) and "Swedish nose" are alternative names.

A range of new, light disposable units are now available which use various arrangements of hygroscopic materials and chemicals. The Engstrom "Edith" uses a lithium chloride coated polypropylene sponge (with chlorhexidine as a bacteriostatic agent); Pall "Ultipor" uses a pleated resin-bonded hydrophobic fibre sheet; Portex "Humidvent" uses a calcium chloride impregnated microporous corrugated paper; and Siemens SH 150 and SH 151 devices use cellulose sponge with a nylon felt insert. Terumo "Brethaid" although disposable, is of the older multiple gauze type. The Pall "Ultipor" is also an effective in-circuit bacterial filter in the intensive care setting.

These new material HMEs are capable of providing up to 30 mg/L AH at 27-30 °C. While they are useful in anaesthesia and for short-term spontaneous or controlled ventilation in the ICU, they are still not satisfactory alternatives to heated humidifiers for long-term ventilation. Airway humidification may not always be adequate, resulting in endotracheal tube occlusions. Humidification is decreased if air leak around the endotracheal tube is significant, especially when used for neonates.

3. Cold Water Bubble Humidifier

An unheated bubble unit screwed directly onto an oxygen flowmeter delivers partially humidified oxygen with water content less than 9 gm/m^3 (i.e. about 50% RH at ambient temperatures). It is inefficient and presents risks of microbiological contamination. Routine use of cold water humidifiers in ICUs to deliver oxygen by simple face masks should not be necessary.

4. Water Bath Humidifiers

With these devices, inspired gas is driven over or through a heated water reservoir. In order to achieve an adequate inspired humidity, the reservoir may be heated to 45-60 °C so that the gas leaving the humidifier contains more than 43 g/m^3 of water, although not fully saturated. As the gas passes along the delivery tube, cooling occurs and the RH approaches 100%. If the reservoir heater is thermostatically controlled to produce an inspired gas

temperature close to 37 °C at the patient end of the delivery tube, then the delivered gas will be fully saturated at this temperature. It is commonly believed that water bath humidifiers do not produce aerosol, but there is now conflicting opinion. Micro-droplets mostly under 5 microm in diameter has been reported with these humidifiers.

Although efficient, hot water humidifiers present the following problems in usage.

(a) Thermostats may not allow fine control of water temperature. Failure may occur. Temperatures above 41 °C are likely to damage the trachea. Continuous supervision by the bedside ICU nurse is necessary.

(b) Condensation occurs from the cooling of inspired gas in the delivery tube. This problem is reduced by lagging of the delivery tubes, and overcome by heated delivery tubes. Nonetheless, a water trap should be installed in the circuit, and the humidifier should always be placed below the endotracheal tube to avoid flooding of the airway by condensed water.

(c) Efficiency is not constant. Gas temperature and humidity is dependent on gas flow rate, surface area of the vaporizing surface, and water temperature. A large vaporizing surface increases RH but the internal compliance of the humidifier is also increased.

(d) Infection is a hazard.

Despite the disadvantages, hot water humidifiers are the most commonly used method of providing humidification in the ICU. Two examples are:

(a) *Fisher-Paykel Humidifier*

This humidifier increases vaporizing surface area without significantly addint to internal compliance to the breathing system. The inspired gas passes over an aluminium spiral scroll lined with absorbent paper within a disposable humidifying module. The reservoir temperature control is variable for flows in the range 3-25 L/min. The delivery tube is heated by an insulated heating wire, adjusted manually to achieve a patient delivery temperature close to 37 °C, and RH about 90%. An additional servo controller unit can be fitted to the Series 328. It senses and indicates delivery temperature and controls the temperature of the heating wire. Audible alarms indicate sensor disconnection and variation of greater than 2 °C of set delivery temperature. The Dual Servo unit combines the heater base and servo controller into one unit.

(b) *Grant Humidifier*

This humidifier uses a simple heated reservoir tank with no attempt made to saturate the inspired gas initially. The water in the tank is maintained at a constant elevated temperature such that the gases leave the tank with a temperature of 41 °C and an RH of about 80%. The inspired gas undergoes a controlled temperature drop along the delivery tube (achieved by a spiral heating element embedded in the tube) so that it is delivered to the patient fully saturated and at body temperature. A platinum resistance sensor at the delivery point regulates the delivery tube heater, thus achieving a low thermal inertia system with a

rapid response. There is built-in compensation for changes in gas flow rate and ambient temperature, as well as fail-safe alarms for both tank and delivery tube heaters.

5. Aerosol Generators (Nebulizers or Atomisers)

These devices deliver micro-droplets of water suspended in a gaseous medium. The quantity of water delivered is not limited as vapour by gas temperature, and super-saturation of the gas is possible (with ultrasonic nebulizers). Aerosols are more stable if the micro-droplets are smaller in diameter, the humidity of the carrier gas is greater, and the surface tension is increased (i.e. by the addition of propylene glycol). Aerosols are used to achieve humidification as well as deposition of water and medications in peripheral airways.

It is generally accepted that particles smaller than 1 microm reach the alveoli, those of 5 microm are deposited in bronchi, and larger micro-droplets of 7-10 microm are deposited in the nose or oropharynx. The types of aerosol generators are:

(a) *Gas-driven nebulizer*. The droplets produced have a size range of 5-20 microm.

(i) A high pressure gas issues as a jet through a fine nozzle which is close to the tip of another tube immersed into the water reservoir. A Bernoulli suction effect draws up the water which is broken up into a fine spray. Smaller microdroplets are produced by directing the jet spray onto an anvil or baffler (i.e. Bird and Puritan nebulizers).

(ii) Another method of producing gas-driven nebulization uses a high pressure jet placed within a fine film of water held in place by surface tension. The film of water is continuously renewed and an anvil of baffle is again incorporated (i.e. Win Liz nebulizer). Mist density is increased when the water reservoir is heated, otherwise gas-driven nebulizers are generally disappointing in clinical use.

(b) *Mechanical (Spinning disc)*

Water is drawn up from the reservoir by an Achimedean screw and impinges onto a spinning disc which flings water micro-droplets into the delivery system by centrifugal force. A spectrum of micro-droplets sizes with low mist density is produced.

(c) *Ultrasonic nebulizer*

These devices utilizes piezo-electric crystal transducers vibrating at radiofrequencies. There are two types:

(i) where drops of water are added onto the surface of the trasnducer;

(ii) where a layer of water lies on top of the transducer.

There is no need for provision of either heating or a high pressure gas source. Smaller, more uniform microdroplets (less than 5 microm) are produced capable of giving a very high mist density of 100-200 g/m^3. The disadvantages of ultrasonic nebulizers are the risk of infection, overhydration and increased airway resistance.

Hazards of Humidifiers

Safe use of humidifiers demands an understanding of the principles of humidification, adherence to the manufacturers' directions for use, close monitoring of the patient and equipment, and a knowledge of potential hazards.

1. Infection

All types of humidifiers are subject to bacterial contamination. Water reservoirs have frequently grown *Pseudomonas* which multiply rapidly at 45 °C. Generation of aerosols from water bath humidifiers (previously thought not to occur), may deposit organisms from the water reservoir to the lungs. In some humidifiers, infection can be controlled by an operating temperature of 60 °C (continuous pasteurization) or by adding 0.02% chlorhexidine gluconate. With all humidifiers, the water reservoir and tubing should be changed every 24-48 hours.

Aerosol generators are potential sources of infection. Bacteria can be carried in water microdroplets to the alveoli, particularly with ultrasonic nebulizers. Nebulizers can also be difficult to clean and sterilize. All units should be replaced and sterilized daily. Sterile water only should be used for refilling the reservoir.

From studies with the Servo devices, the newer, condenser HMEs do not appear to increase the risk of infection from airborne organisms, despite the devices becoming heavily bacteria laden.

2. Overhydration

Fluid overload from alveolar absorption is most relevant with the use of ultrasonic nebulizers in paediatric practice. "Drowning" with condensed water is avoided with heated delivery tubes and by positioning the humidifier below the tracheostomy or endotracheal tube.

3. Overheating

A constantly elevated inspired gas temperature can contribute to hyperpyrexia. Correct functioning of the thermostat and alarms, and monitoring of the inspired gases at the patient end should avert scalding of the patient's trachea. A delivered gas temperature of 35 °C is satisfactory and provides an adequate margin for safety.

4. Electrical Hazards (See Chapter 75, Electrical Injuries).

Chapter 25: Adult Respiratory Distress Syndrome

T. E. Oh

The adult respiratory distress syndrome is a form of respiratory failure resulting from a variety of direct and indirect pulmonary injuries, all of which present with similar pathophysiological changes. Names which have been used for this syndrome include "wet lung", "shock lung", "post-traumatic pulmonary insufficiency", "adult hyaline membrane

disease", "ventilator lung" and "pump lung". The syndrome is characterized by a clinical picture of marked respiratory distress, diffuse pulmonary infiltration on chest radiography, reduced pulmonary compliance and marked increase in alveolar-arterial oxygen difference (A-aDO_2) (Table 1), and is now most commonly known as the adult respiratory distress syndrome (ARDS).

Aetiology

A list of clinical conditions which have been implicated in the causation of this syndrome is shown in Table 2. These may affect the lungs directly (i.e. aspiration) or indirectly (i.e. sepsis). Shock is not a prerequisite for the development of ARDS. Major risk factors appear to be sepsis, aspiration, lung contusion, and multiple fractures. The true incidence is unknown and may be only 7% of at risk patients.

Pathophysiology

A proposed pathophysiological process of ARDS is shown in Figure 1. Pulmonary endothelial injury, "capillary leak", and surfactant abnormalities result in interstitial and alveolar oedema. Attenuated alveolar type I cells are lost and replaced by cuboidal microvillous Type II cells resulting in thickened alveolar walls. The interstitium becomes infiltrated with inflammatory and other cells, while many alveoli are filled with proteinaceous and haemorrhagic fluid debris. Hyaline membrane, focal atelectasis, and capillary micorembolism are common findings. Pulmonary fibrosis appears and progressively obliterates pulmonary architecture, including the microvasculature.

The pathological changes result in reduced functional residual capacity (FRC), increased shunt effect, reduced lung compliance, and gross hypoxaemia. The role of abnormal surfactant is speculative. Bronchoalveolar lavage fluids from ARDS patients have demonstrated abnormally aggregated and inactive surfactant.

Pathogenesis

The mechanism of lung damage is controversial, but the concept of "non-cardiogenic capillary leak" is over-simplified. Post-mortem, clinical and animal studies have suggested certain hypotheses, the two most significant are discussed below. However, no mechanism or common factor has been established as a common pathway to the acute lung injury of ARDS.

1. Complement Activation

ARDS has been suggested to be initiated by complement activation, a common consequences of predisposing events. Complement activation causes leuocyte sequestration in pulmonary capillaries. The aggregated neutrophils injure endothelial cells through unknown mechanisms which liberate toxic oxygen (superoxide) radicals, arachidonic acid metabolites, and proteases. In addition, the proteases destroy structural proteins (such as collagen, elastin, and fibronectin) as well as plasma proteins (thus promoting further local inflammatory changes). Normal pulmonary antiproteases, i.e. alpha1 antitrypsin are inactivated by oxygen radicals, leading to increased injury.

Complement activation has been shown in sheep experiments, and the presence in plasma of a peptide product of activated complement, C5a, has been reported to accurately predict ARDS. Broncho-alveolar lavage (BAL) studies have detected the presence of neutrophils, proteolytic enzymes, chemotactic factors and abnormal antiproteases in lavage washings.

2. Fibrinolysis and Platelet Aggregation

Activation of the clotting system may be a causative mechanism of ARDS from trauma. ARDS may be related to intravascular coagulation and platelet aggregation. Disseminated intravascular coagulation (DIC) is a common finding in ARDS. Platelet-fibrin thrombi have been found in post-mortem lungs of patients with ARDS. The platelet-fibrin micro-emboli release vasoactive substances, such as serotonin and prostaglandins. Fibrinolysis produces fibrinogen degradation products (FDPs) which together with vasoactive substances, may injure endothelium and pulmonary microvasculature. The FDP "D antigen" has been identified in patients who develop ARDS and may be a marker or mediator of injury.

Both hypotheses, however, suffer from sparse clinical evidence. Complement activation is non specific and has no predictive value. ARDS may develop in neutropaenic patients (i.e. without neutrophil activation). BAL findings are non specific, and from the airway endothelium, which may be different from the vascular endothelium. The pathogenesis may be multifactorial, with complement and neutrophil activation, reticular endothelium system dysfunction, and direct toxicity of endotoxin, oxygen and other factors being implicated.

Clinical Presentation

The syndrome usually develops insidiously 24-72 hours following the precipitating event. The usual features are dyspnoea, tachypnoea, cyanosis and fine crepitations in both lung fields. Arterial blood gases reveal severe hypoxaemia and an increased A-aDO_2. Chest radiography shows widespread, diffuse opacification. As the disease progresses, lung compliance decreases and the dead space:tidal volume ratio increases. An increasing minute volume is required to maintain an adequate arterial PaO_2.

ARDS may develop in patients who are already on mechanical ventilation, and is manifested by the deterioration of the above pulmonary function parameters.

Management

Treatment is directed against the precipitating conditions, but is otherwise empirical and supportive.

1. Mechanical Ventilatory Support

The mainstay of treatment is mechanical ventilatory support via na endotracheal tube or a tracheostomy if ventilation is prolonged. Continuous mechanical ventilation (CMV) using intermittent positive pressure ventilation (IPPV) may be used. Alternatively, some spontaneous breathing component, i.e. intermittent mandatory ventilation (IMV) or pressure support may

be used. This may help reduce mean airway and intrathoracic pressure and be advantageous in some patients. The optimal mode of ventilation is not known.

If oxygenation cannot be maintained at an adequate level with an inspired oxygen concentration less than 60%, then positive end expiratory pressure (PEEP) should be used. PEEP helps recruit or maintain open lung units that are otherwise collapsed, and partly restores the reduced FRC, thus improving oxygen transport across the lung. PEEP does not, however, decrease lung water and this is not a mechanism for gas exchange improvement. Early "prophylactic" use of PEEP does not prevent the development of subsequent progress of ARDS. A range of 5-15 cm water (0.5-1.5 kPa) of PEEP is usually used. The benefits of PEEP are counterbalanced by the decreased cardiac output and increased risk of barotrauma. Higher levels of PEEP have been advocated, but better results have not been consistently substantiated, despite the increased advantages.

The optimal level of PEEP is controversial. "Best" or "optimal" PEEP has been reported to mean various levels, producing:

(a) the lowest shunt, i.e. venous admixture below 20% cardiac output;

(b) the maximum oxygen delivery to tissues;

(c) adequate arterial oxygenation at the lowest inspired oxygen concentration; and

(d) maximum improvement in lung compliance.

The minimal level of oxygen necessary to achieve adequate oxygenation (i.e. PaO_2 of approximately 60 mmHg, 8.0 kPa) should be supplied. Oxygen in high concentrations is toxic to the lungs. PEEP allows reduction of inspired oxygen, which should if possible, be kept below 50%. Nevertheless in critically hypoxaemic patients, PEEP as well as 100% oxygen may be required. PEEP should thus be adjusted to produce the "optimal" clinical improvement, with monitoring of haemodynamic, respiratory and oxygenation variables.

Recent developments in high frequency ventilation may minimize mean intrathoracic pressure, but do not appear to reduce mortality.

2. Fluid Management

Fluid administration must be carefully controlled to allow improvement of systemic and pulmonary perfusion without aggravating the pulmonary oedema. Central venous pressure monitoring may be adequate, but a more reliable guide to fluid management is the measurement of pulmonary capillary wedge pressure (PCWP) using a Swan-Ganz catheter. Indeed, it is necessary to measure PCWP to properly diagnose ARDS. The choice of fluid replacement remains controversial. Colloid replacement to restore the Starling relationship (Table 3) between hydrostatic and colloid osmotic pressure is commonly used.

The use of concentrated salt-poor albumin with concomitant diuretic (frusemide) therapy is believed to be benficial. Plasma colloid osmotic pressure is elevated, which may aid in removing extravascular lung water. Concentrated albumin infusion also allows fluid and

salt restriction without significant haemodynamic deterioration. However, it has also been suggested that extravascular lung water may be increased with the use of colloid compared with crystalloid infusions. Clinically, there appears no advantage in the of colloid or crystalloid.

Table 3. The Starling Equation

$$F = K ((P_c - P_i) - (II_c - II_i))$$

F = Fluid flux favouring extravasation of fluid
K = Membrane permeability coefficient
P_c = Pulmonary capillary pressure
P_i = Interstitial space hydrostatic pressure
II_c = Capillary colloid osmotic pressure
II_i = Interstitial space colloid osmotic pressure

3. Cardiac Support

Optimal preload is achieved with fluid administration according to the PCWP. Inotropic agents such as adrenaline, dopamine or dobutamine are necessary in circulatory failure. Vasodilators are used by some to decrease afterload. There has been recent interest in pulmonary hypertension in ARDS, which signifies a poor prognosis, and attempts to reduce the pulmonary arterial pressures have not met with significant success.

Since many treatment variables are involved, serial cardiac output and shunt fraction estimations, and continuous mixed venous oxygen saturation monitoring are useful to derive optimal fluid and inotrope delivery as well as ventilation settings, especially PEEP. It is important that oxygen transport is optimized, as oxygen consumption in ARDS appears to be *dependent* on oxygen delivery. Hb should be kept at 12-13 g/dL, and hypophosphataemia (for 2,3-DPG) and systemic alkalosis avoided.

4. Nutrition

Adequate nutrition should be supplied to minimize muscle wasting and immune deficiency.

5. Physiotherapy

Physiotherapy, adequate removal of secretions and frequent posture changes of the patient are important. Self-sealing endotracheal tube adaptors are necessary for tracheal suctioning of patients ventilated on PEEP.

6. Other Therapeutic Consideration

(a) *Corticosteroids*

The use of corticosteroids is controversial. Steroids may reduce lung injury by inhibiting complement-induced leucocyte aggregation, and reduce capillary permeability if

used early for a short period (i.e. 1-2 g methylprednisolone/day for 24-48 H). There is however, the potential effect of reducing host defences with increased mortality, and the role of steroids in ARDS awaits further confirmation.

(b) *Positive airway pressure*

Continuous positive pressure breathing with spontaneous ventilation (i.e. continuous positive airway pressure) has been used in the management of ARDS. However, many patients in severe respiratory distress cannot tolerate this mode of ventilatory support.

(c) *Antibiotics*

The specific antibiotic should be used for organisms cultured, including anaerobic organisms. Blind use of prophylactic broad spectrum antibiotic cover should be avoided.

(d) *Heparinization*

This will depend on criteria for the diagnosis of DIC and not for ARDS.

(e) *Extracorporeal membrane oxygenators (ECMO)*

The use of ECMO for prolonged periods has been disappointing, resulting in the same mortality as that of conventional treatment. A combination of ECMO (for CO_2 removal) and low frequency ventilation to provide oxygen uptake has also been reported (LFPPV an ECCO2R).

(f) *Ultrafiltration*

The use of ultrafiltration (with or without renal dialysis) to remove interstitial water, may be indicated in patients less responsive to diuretics. It has been reported to be useful in septic patients with ARDS, postulated to be due to the removal of harmful vasoactive peptides. More clinical evaluation is however, required.

(g) *Experimental agents*

There is interest in using various pharmacological agents to inhibit postulated pathogenetic pathways of ARDS or vasoactive mediators. Hence vasodilators, prostacyclin, prostaglandins, ketanserin, fibronectin, free radical scavengers, non-steroidal antiinflammatory drugs, and damazol have been tried with no real clinical success. Many therapeutic mechanisms are speculative and, at best, warrant clinical trials.

Outcome

Patients with ARDS may recover. Otherwise progressive deterioration, commonly accompanied by sepsis, coagulopathy, and multi-organ failure, lead to death within 3-4 weeks. Death is attributed to multi-organ failure via septic mechanisms, rather than hypoxaemia per se. The mortality rate of over 50-60% has remained unchanged over the last decade despite

advances in treatment modalities. Present poor figures may be a result of the stringent diagnostic criteria of ARDS today. Most survivors have normal lung function although abnormalities in gas transfer persist. Other survivors have a reduction in vital capacity and obstruction of air flow.

Chapter 26: Pulmonary Embolism

T. E. Oh

Pulmonary embolism (PE) is a complication of deep vein thrombosis (DVT). The actual incidence is difficult to ascertain, but may be as high as 630,000 cases annually in the USA. It is a frequent cause of morbidity and mortality in both postoperative and medical patients. In autopsy reports, death has been directly attributed to PE in 15% of cases. The mortality in treated patients is significantly lower than those undiagnosed or untreated. Hence, prophylactic measure against DVT, and early diagnosis and treatment of PE is important, especially in critically ill ICU patients.

Aetiology

Almost all pulmonary emboli result from frequently asymptomatic thromboses from deep veins of the lower limbs, pelvis and inferior vena cava (proximal DVT), and rarely from thromboses in the upper limbs, right atrium or ventricle. Thrombosis limited to calf veins (distal DVT) seldom results in clinically obvious PE, but progression to a proximal thrombus and direct embolization from a calf-only thrombus are possible.

Predisposing factors for thrombosis are best considered in terms of Virchow's triad (a) stasis of blood flow, (b) damage to vessels, or (c) alterations in coagulation mechanism (Table 1). High risk patients for DVT and PE are those with heart failure, cancer, prolonged bed rest, obesity (especially females), and hip fracture, and aged over 65 years and receiving oestrogen therapy. Other less well known, but significant risk factors are heritable disorders. Inherited deficiencies of protein C, protein S, and antithrombin III (ATIII) have recently been discovered. Protein C and S are vitamin K-dependent antithrombotic proteins. Inherited abnormalities of fibrinogen and plasminogen also increase the risk of PE.

Clinical Presentation

Pulmonary embolism has a varied non-specific presentation, largely dependent on the severity and multiplicity of the embolic episode. Symptoms and signs may be mistaken for manifestations of coexistent diseases. Such diseases of the heart and lungs is likely to influence the outcome of PE. Small "herald" emboli may precede a major embolus by days or weeks. The majority of emboli are multiple.

1. Symptoms

The most common symptom is dyspnoea of sudden onset (85% of patients). Chest pain of substernal or pleuritic type occurs in 70%, and apprehension and non-productive cough occur in 60% of cases. Syncope (14% of patients) is usually only associated with massive

pulmonary embolism. Classic symptoms of pleuritic pain and haemoptisis are not early symptoms and are present only if infarction has occurred (10% of patients).

2. Physical Signs

There may be no helpful clinical signs. Those present are usually non-specific and include:

(a) *Respiratory*

Tachypnoea with shallow breaths (> 20/min) is seen in 80% of patients. Cyanosis is usually restricted to cases of massive embolism. A pleural effusion and friction rub may be found if infarction has occurred, usually in the lower lobes. Wheezing is present infrequently. Rales may be a manifestation of coexisting cardiopulmonary disease.

(b) *Cardiovascular*

Tachycardia (> 100/min) may relate to the site of the obstruction. Onset of bradycardia is an ominous sign. Accentuation of the pulmonary valve closure sound and widened splitting of the 2nd heart sound may reflect a rise in pulmonary arterial pressure. Mean pulmonary artery pressure is elevated by 5 mmHg (0.67 kPa) when more than 50% of the pulmonary vasculature is acutely obstructed. A right ventricular heave may be palpable. S_3 and S_4 gallop heart sounds may be detected, often associated with extensive embolism. A high jugular venous pressure and prominent "a" waves may be seen. Systemic hypotension and shock occur in the presence of massive embolization; a small sharp peripheral pulse may be palpated.

(c) *Lower Limbs*

Clinical evidence of DVT may be present, but is found in only about 30% of patients with PE. A "normal" leg may give rise to emboli, more so than an overly thrombophlebitic (calf-vein thrombus) leg.

(d) *Other Signs*

A modest fever (38-39 °C) is found in 45% of patients, and diaphoresis in one third.

Many of the above signs may be transient and persist for only a few hours after the acute embolization, perhaps signifying early lysis and fragmentation, with more distal distribution of the embolus. The pathophysiological bases of the clinical features are shown in Table 2. Differential diagnosis includes myocardial infarction, acute left ventricle failure, aspiration pneumonitis, acute pneumonia, fat embolism, pneumothorax, and dissecting aortic aneurysm.

Investigations

Objective diagnostic tests are essential, as the clinical examination and readily available tests (i.e. chest X-ray) are unreliable to diagnose or exclude PE. Investigation include those to diagnose DVT as well as PE.

Diagnosis of DVT

About 90% of pulmonary emboli are thought to arise in the deep veins of the lower extremities and pelvis. Diagnosis of DVT may help to diagnose PE, if specialized facilities to confirm PE are unavailable, and also in the decision to use thrombolytic therapy. Studies of the lower extremities for DVT are:

1. Radiolabelled Fibrinogen Scan

Radioisotope I^{125} fibrinogen is injected IV and the legs are scanned for up to 7 days. The test is good to detect calf-vein (distal) thrombi, but relatively insensitive for thrombi in the thigh and pelvis. It is also only effective prospectively, i.e. when the thrombosis is still developing, and has to be performed over several days.

2. Impedance Plethysmography

This is a new noninvasive technique sensitive for proximal, but not distal DVT. Electrical impedance is measured distally, during inflation and deflation of a mid thigh pneumatic cuff. Change of impedance reflects change in blood volume, indicating venous obstruction. Diagnostic reliability has been verified with serial impedance plethysmography over 10-14 days. This combined with fibrinogen leg scanning, is equal in sensitivity to invasive venography.

3. Doppler Ultrasonography

Doppler ultrasound detects flow changes in veins. The technique is sensitive for obstruction of popliteal and more proximal veins. However, interpretation is subjective.

4. Contrast Venography

Venography is the most accurate diagnostic technique. However, visualization of external and common iliac veins may be inadequate in some patients. A negative venogram cannot exclude a DVT with utmost certainty, as embolism may have arisen from sources other than the lower extremities. It is invasive and expensive, and complications inslude pain and a very low incidence of DVT itself.

Diagnosis of PE

Diagnostic investigations include routine laboratory and bedside tests, although these are generally non specific.

1. Blood

White cell count may be elevated (> 15,000 x 10^6 cells/L). Serum lactic dehydrogenase, transaminase enzymes and billirubin levels may rise infrequently and late in the illness. However, they lack specificity to be of any use in the acute situation. The elevation of fibrinogen degradation products is currently more of research than clinical interest.

2. Chest X-ray

This is not specific or diagnostic, but comparison with previous films may be helpful. The chest film may be normal. Focal pulmonary oligaemia, localized infiltrates, consolidation, raised diaphragms, pleural effusion, and "plump" pulmonary arteries are seen in up to half the cases.

3. Electroencephalograph

The classic pattern of a deep S-wave in lead I, and a Q-wave and inverted T-wave in lead III (S1Q3T3) is not frequently seen. Non-specific S-T depression and T wave inversion in anterior leads is the most common finding, reflecting right heart strain. P pulmonale, right bundle branch block, and atrial arrhythmias are also occasionally present, and persistent if embolization is massive. A normal ECG is present in 6% of cases with massive embolization. The ECG may be useful, however, in excluding acute myocardial infarction.

4. Arterial Blood Gases

Hypoxaemia is frequently present, but an arterial PO_2 over 80 mmHg (10,6 kPa) is not uncommon in PE. Hypocarbia may be present, as a result of the tachypnoea. It is important to know the inspired oxygen concentration at the time of arterial blood sampling. Metabolic acidosis will be present if a shock state follows a large embolus.

5. Ventillation/Perfusion Lung Scans

A perfusion lung scan (using IV technetium-99m labelled albumin) is a sensitive non-invasive test which should be performed whenever PE is suspected. Perfusion defects may be classified as single or multiple, and as subsegmental, segmental, or lobar. A ventilation scan (inhalation of xenon-133) performed in conjunction, markedly improves specificity over a perfusion scan alone. Defects may "mismatch" (with normal ventilation at the site of a perfusion defect) or "match" (when the ventilation defect corresponds with the perfusion defect). The probability of PE may be deduced from V/Q lung scans as being high, low, or intermediate (Table 3). Presence of pre-existing lung disease makes interpretation of V/Q abnormalities difficult, and false positive findings may be made. The diagnostic value of the low probability category is currently debatable; 25-40% of such cases show abnormalities on subsequent angiography. Nevertheless, general management guidelines based on V/Q lung scans are possible.

(a) A normal perfusion scan virtually rules out significant PE.

(b) A high probability V/Q scan with significant risk factors reliably establishes the diagnosis of PE.

(c) A low probability V/Q scan with a high clinical index of suspicion warrants pulmonary angiography.

(d) A high probability V/Q scan with normal non-invasive tests for DVT and low risk factors should also be confirmed by pulmonary angiography.

(e) V/Q lung scans are used to document resolution of confirmed emboli.

6. Pulmonary Angiography

This is a specific "gold standard" test. Unfortunately, it is invasive and specialized, with an associated mortality and morbidity (albeit small and probably less than that of empirical anticoagulation). A positive angiogram shows consistent defects in multiple films or sharp cut-offs in vessels over 2.5 mm diameter. Massive PE produce significant filling defects or obstruction in 2 or more lobar arteries. Indications for pulmonary angiography include the above considerations with V/Q scans, confirmation of PE in a patient at increased risk of bleeding from anticoagulants, and massive PE to decide choice of thrombolytic, embolectomy, or vena caval interruption therapy. The pulmonary angiogram catheter can be left in situ for measurements of pulmonary arterial pressures, direct infusion of thrombolytic drugs and repeat angiography.

7. Angioscopy

A pulmonary fiberoptic angioscope is directed percutaneously via the jugular vein into the heart and pulmonary arteries. Direct visualization of pulmonary arteries from the main trunk to 3.5 mm diameter vessels is then possible. This new technique may be helpful when the diagnostis remains equivocal or if the patient is allergic to angiographic contrast media. It may also help to identify and localize suspected chronic pulmonary emboli.

Management

General Measures

General measures in the acute situation include oxygen therapy, haemodynamic support, and treating shock in massive PE. Cardiopulmonary resuscitation is undertaken in acute cardivascular collapse.

1. Oxygen Therapy

Oxygen is given by mask. High flows should be used because air entrainment from marked hyperventilation will result in a lower than expected inspired oxygen concentration. Intubation and mechanical ventilation may be necessary.

2. Haemodynamic Support

It is imperative to maintain right heart filling pressures. Elevation of the lower limbs will increase venous return by autotransfusion, and thus assist right heart filling pressures (Starling effect). Placement of a Swan-Ganz catheter, although not essential, will enable monitoring of responses to vasoactive and thrombolytic agents. Fluid infusion and positive inotropes may help to maintain systemic and pulmonary circulations. Isoprenaline, although a potent inotrope and pulmonary vasodilator, is less useful, as it is also arrhythmogenic and a systemic vasodilator (and thus decrease right heart filling pressures). Femoro-femoral partial cardiopulmonary bypass has been used to support the circulation until thrombolytic therapy or embolectomy can be undertaken.

Radiographic contrast injection can cause systemic vasodilation and a decrease in right heart filling pressures, with possible catastrophic effects. Atropine and phenylephrine should be readily available. An intravenous line should be inserted in the left arm as angiographic procedures are usually performed from the right arm.

Definitive Therapy for DVT and PE

Definitive treatment is directed towards prevention of new thrombus formation, thrombolysis, blocking migration of emboli, and emboli removal.

1. Heparin Therapy

Heparin enhances the inhibitory effect of ATIII on thrombin and Factor Xa. Heparin anticoagulation by infusion is safer and more efficacious than intermittent IV bolus doses for preventing new thrombus formation. A bigger IV bolus of 15,000-20,000 units is advocated, followed by an infusion of 1000-1500 units/h. Heparin is known to antagonize platelet-released serotonin and histamine, which are known to cause acute pulmonary vasoconstriction, and further exacerbate pulmonary hypertension associated PE.

The dose of heparin is adjusted to maintain partial thromboplastin time (APPT) at 1.5-2.5 times the control level. Heparin anticoagulation may be achieved in a patient with ATIII deficiency by simultaneous administration of plasma to provide exogenous ATIII. Therapy is usually continued for 7-10 days with a 5 day overlap with the start of oral warfarin therapy. Starting warfarin soon after heparin (even the same day), with a similar 5 day overlap, reduces exposure to heparin and is reported to be effective and safe.

Heparin may induce thrombocytopenia and a paradoxical thrombotic thrombocytopenia syndrome. In severe cases, heparin should be discontinued, and other treatment measures instituted.

2. Warfarin Therapy

Warfarin and other coumarin derivatives inhibit synthesis of vitamin K-dependent clotting factors, i.e. prothrombin and Factors VII, IX and X. In addition, it reduces anti-thrombotic protein C levels. Thus, during the early stages of warfarin therapy, a hypercoagulable state may exist, before all vitamin K-dependent factors with longer half-lives

(II, IX and X) are sufficiently inhibited. Hence, heparin therapy must continue for 5 more days after the start of warfarin, even though the prothrombin time may reflect a therapeutic warfarin effect after 2-3 days.

The usual loading dose is 25-30 mg given over 36 hours. Maintenance is often about 5 mg/day but must be controlled by regular prothrombin time estimations (at about 2 times control) or international normalised ratio (INR, 2-3). Haemorrhage is the important side effect of warfarin anticoagulation. Age increases the bleeding risk. Interaction with other drugs (i.e. salicylates, phenothiazines and phenylbutazone) potentiates the action of warfarin. Haemorrhage from warfarin toxicity may occur into kidneys, gastrointestinal tract, lungs, subdural or subarachnoid space, skin, mucous membranes and muscles. Bleeding into the retroperitoneal space is often insidious.

Oral warfarin therapy and monitoring is continued for 1.5-3.0 months for DVT and 3-6 months for PE, and longer in patients at particular risk - one year in those with a previous DVT, and indefinitely if more than 2 episodes of PE have occurred. Contraindications to anticoagulation are given in Table 4. Poor patient compliance with regular medication, and trauma-prone occupation affect long-term anticoagulation.

Table 4. Possible Contraindications to Anticoagulant Therapy

Peptic ulceration
Hiatus hernia
Hepatic disease
Steatorrhoea
Hypertension
Retinopathy
Infective endocarditis
Uraemia
Alcoholism
Pregnancy
Recent surgery and trauma
Cerebral haemorrhage
Haemostatic defect
Poor patient compliance

Reversal of warfarin therapy, if indicated is achieved with vitamin K. A small dose of 5 mg will shorten the prothrombin time. Complete reversal of anticoagulation requires a larger dose, i.e. up to 50 mg. However, if anticoagulation is to be interrupted for an elective surgical procedure, it is best to withhold warfarin for about 3-4 days beforehand. Vitamin K administration will make the control of prothrombin time difficult on recommencement of warfarin, for 2-3 weeks. Acute reversal of warfarin therapy is best achieved by administration of fresh frozen plasma and factor concentrates.

3. Thrombolytic Therapy

Thrombolytic therapy may accelerate resolution of emboli and improve cardiopulmonary status, but improvement in total mortality from PE has not been

demonstrated. Nevertheless, thrombolytic therapy is reasonable for extensive proximal DVT, PE with haemodynamic instability, and a perfusion defect of one lobe or greater.

Streptokinase and urokinase activate plasminogen to form plasmin, thereby promoting clot lysis. Streptokinase, despite its potential pyrogenic and antigenic properties, is usually used. It has a MW 43,000, and is rapidly bound to the patient's previously generated circulating antistreptococcal antibodies. Thus a dose must be sufficiently large to provide a free excess for fibrinolytic activity. The dose required may be calculated in vitro. A typical regimen is: 250,000-600,000 units loading infusion over 30 min, followed by an infusion of 100,000 units/h for 24 hours. Longer therapy (3-7 days) may result in better improvements in the pulmonary and leg deep venous circulations. Antihistamines and hydrocortisone (100 mg before and then each 12 hours of therapy) will reduce immunological reactions. High fevers and rigors are generally uncommon. Adrenaline and resuscitation equipment should be immediately available.

Urokinase has a more rapid onset of action, is non-antigenic and may be used repeatedly, but remains very expensive. It is given 4400 units/kg IV over 10 min as a loading dose, followed by an infusion of 4400 units/h for 12 hours.

Monitoring is achieved by thrombin clotting time (2-4 times the control) and euglobulin lysis time measurements; before therapy, at 4 and 8 hours after commencement for urokinase, and 4 and 12 hours after commencement for streptokinase. Consultation with a haematologist is recommended. Heparin infusion is recommended after the course of thrombolytic therapy is complete.

Main disadvantages of streptokinase therapy are bleeding and allergic reactions. Contraindications to the use of streptokinase or urokinase are given in Table 5. Intramuscular injections must be avoided (as with heparin therapy) and blood sampling minimized and restricted to sites where digitial compression is possible. If complications occur, streptokinase infusion must be stopped (half-life of 15 minutes). If necessary, fresh frozen plasma is given to replenish depleted coagulation factors. Epsilon aminocaproic acid (amicar, 5-8 g) or aprotinin (trasylol; 500,000 units) have been used to antagonize streptokinase fibrinolytic action more rapidly.

New clot-specific thrombolytic agents with less systemic fibrinogenolysis than streptokinase or urokinase have recently been introduced. These include APSAC (anisoylated plasminogen streptokinase activator complex) and rTPA (recombinant tissue plasminogen activator). They have been studied more in acute coronary thrombosis, but also appear to be more beneficial than the first generation thrombolytics.

4. Inferior Vena Cava (IVC) Filter

Placement of a mechanical barrier to migration of emboli in the IVC should be considered, if development of a new PE might prove fatal. The indications are:

(a) Recurrent PE despite adequate anticoagulation.
(b) Inability to tolerate anticoagulation.
(c) A large, free-floating thrombus in the ileo-femoral veins.
(d) Immediately following pulmonary embolectomy.

The Greenfield filter is commonly used, placed transvenously under fluoroscopic guidance. It can achieve recurrent PE rates of 5%. Heparin should be started 12 hours after placement of filter in those without contraindications to anticoagulation.

5. Embolectomy

Surgical embolectomy is uncommon, because most patients with massive PE respond well to conservative therapy. Data on its usefulness is unavailable. Specific criteria for pulmonary embolectomy are difficult to derive. Cardiovascular improvement following streptokinase therapy is similar to that of pulmonary embolectomy with cardiopulmonary bypass, but has a higher morbidity and mortality. However, if streptokinase therapy is contraindicated or unsuccessful, and there is persistent hypotension, oliguria, hypoxia, and metabolic acidosis, with radiological confirmation of greater than 50% occlusion of the pulmonary arterial tree, then pulmonary embolectomy may be all there is to offer. This may be attempted by open thoracotomy or by special transvenous catheters. Venous thrombectomy on the lower limbs is rarely undertaken. Consideration is given to venous thrombectomy if indicated by venography, and if the thrombosis formation is recent.

Prophylaxis Against DVT and PE

Prevention of PE is largely the prevention of DVT. Prolonged anticoagulation with oral agents is useful in those patients at high risk of recurrent emboli. In lower risk or preoperative patients, mobilization exercises in addition to low dose heparin (5000 units subcutaneously 2-3 times daily), offers moderate protection. Low MW heparin appears to be as effective, with less risk of bleeding, but is not generally available. Low dose heparin prophylaxis, however, is not always suitable for neurosurgical, ophthalmic, or orthopaedic joint replacement patients. For such patients, intermittent pneumatic compression of the legs may be as effective. It should be initiated in the operating room and continued for at least 3 days or until fully ambulatory. Elastic stockings donned preoperatively improve venous return from lower extremities, and may be beneficial in conjunction with other measures.

Dihydroergotamine increases tone of capacitance vessels. The combination with subcutaneous low dose heparin appears superior to heparin prophylaxis alone. However, alteration of vascular responses in myocardial and peripheral ischaemia remains a theoretical concern. Other modalities tried with some success, include antiplatelet agents (aspirin or dipyridamole), dextran infusion, and two-stage warfarin. In the last approach, warfarin is started 14 days preoperatively (prothrombin time 1.5 longer than control) and dosage is increased postoperatively (prothrombine time 2-3 times control).

Prognosis

The mortality of treated PE is approximately 5%, and largely dependent on the severity of underlying disease. With continued anticoagulants, the long-term prognosis is good; the haemodynamic problems resolve as the embolus lyses (sponatenously or therapeutically). Pulmonary hypertension is probably only associated with recurrent emboli, and almost never after a single episode.

Other Pulmonary Embolic Pathologies

Pulmonary artery obstruction may result fro embolization with bone marrow, fat, tumour (choriocarcinoma and renal vein tumours), air and amniotic fluid. General principles of resuscitation are enacted. A high mortality is associated with major air and amniotic fluid embolization.

Air embolism may result from the aspiration of air into large open veins at operation, or after inadvertent disconnection of large bore central venous catheters. Additional therapeutic manoeuvres include compression/occlusion of the air source, placing the patient in the left lateral, head down tilt position, and placement of a central venous line such that the tip position allows aspiration of air from the right atrium, ventricle or pulmonary artery. Anticoagulation may be required to prevent thrombus forming around residual intra-cardiopulmonary air bubbles. Associated acute pulmonary hypertension may facilitate paradoxical embolus across a patent foramen ovale.

Amniotic fluid embolism often results in catastrophic cardiovascular collapse in conjunction with an acute bleeding diathesis and anaphylactic shock. A central venous catheter is placed to aspirate intracardiac amniotic fluid for confirmation of diagnosis and monitoring of cardiovascular status. Cardiopulmonary resuscitation, fresh blood, coagulation factors and fibrinolytic inhibitors may be required.

Chapter 27: Fat Embolism

P. D. Cameron

Fat embolism is often a contributing cause of death in patients with multiple injuries. Although fat can be found in the lungs of almost all patients involved in major trauma, the clinical syndrome of fat embolism (FES) is found in approximately only 5% of such patients. In one report, 60% of major orthopaedic procedures have been associated with fat globules (of 7-14 microm diameter) passing to the lungs, but without development of the clinical syndrome. FES is more frequently seen in young adults, perhaps due to their predilection to motor trauma, and may be a contributing factor in the adult respiratory distress syndrome. It is less commonly seen in sporting injuries, children and elderly patients. FES may also be associated with systemic lupus erythematosus, pancreatitis, diabetes mellitus, rapid decompression, lymphography, poisoning, hepatic failure, hepatic trauma, sickle cell crisis (from marrow infarcts), extracorporeal circulation and intravenous lipid infusions; but in this group it is usually a post mortem histological finding rather than a clinical syndrome.

Aetiology

The aetiology of FES remains controversial, despite its recognition over 100 years ago and extensive research since. The temporal relationship with fractures is not in doubt. There is also no doubt that patients with FES have embolization of fat macroglobules into both the pulmonary and systemic circulations. However, many patients with long bone and pelvic fractures have embolization of fat, but without clinical evidence of the syndrome.

Source of Circulating Fat in Trauma

1. *Associated with bone fracture* (particularly pelvis or long bones of the leg), rupture of fragile medullary venous sinuses occurs, allowing intravasation of fat and marrow to join the venous return to the heart. Fracture haematoma may further increase intra-medullary pressure and facilitate the entry of fat into the sinusoids. Closed fractures have a higher incidence of FES than do open fractures. Tourniquets placed proximal to the fracture site may delay the passage of fat centrally.

2. *Massive trauma* may disrupt adiopose tissue (especially high velocity projectiles, explosion and extensive burns) causing the entry of large fat globules into the venous circulation. Liposuction has also been associated with fat embolism.

3. *Fat transported in the circulation* is usually emulsified and in the form of neutral triglycerides bound to albumin or low density lipoproteins. In the microscopic form of chylomicrons (of 1 microm in size), they are stable and a major calorie source. Following the stress of trauma, release of catecholamines and corticosteroids occurs, causing increased release of depot fat. Fat stores may be sufficiently mobilized for transport mechanisms to be overwhelmed, and the chylomicrons to become unstable and coalesce into larger (20 microm) particles which ultimately obstruct smaller capillaries. Calcium dependent C-reactive protein may coalesce very-low-density lipoproteins (VLDL) and agglutinate chylomicrons into larger particles resulting in FES and pancreatitis.

Two main theories have been advanced as to the causative mechanism for fat embolisation.

1. Mechanical Theory

This proposes that there is simply a mechanical intraluminal obstruction of capillaries by blood-borne fat globules. It is postulated that not all fat globules are filtered out by the pulmonary circulation, but while in a semi-liquid state, pass through pulmonary capillaries, arteriovenous communications or a patent foramen ovale (present in up to 25% of population), eventually lodging in capillaries of the systemic circulation. Organs with high blood flow (i.e. brain, kidney and heart) often show histological evidence of capillary obstruction by fat.

2. Physiochemical Theory

It is proposed that there is a toxic effect of liberated free fatty acids (FFA) on body tissues. Patients with FES have been shown to have a lower albumin level and a higher lipoprotein lipase level in serum than patients who do not have the syndrome, suggesting the potential for endothelial tissue damage from a high level of free, non albumin-bound fatty acids. Pulmonary lipase can also break down neutral triglycerides into toxic unsaturated FFA.

Various reports have been submitted over the past 50 years supporting one or other theory. It seems likely that both mechanisms are involved to some degree. Experimentally, hypoxia and chemical pneumonitis can be produced by the injection of unemulsified fat (i.e. oleic acid). Radioactive carbon-labelled fat has been shown to pass from fracture sites through the pulmonary capillaries and into the systemic circulation.

Pathophysiology

Irrespective of the aetiology of FES, the main pathophysiological effects are due to blockage of pulmonary and systemic capillaries, either with fat alone, or with associated microaggregates of platelets, red cells and fibrin. It is likely that the pulmonary effects of FES occur in two phases, either of which may be sufficiently severe to result in patient death due to respiratory failure.

1. The firs phase is immediate in onset and associated with mechanical obstruction of pulmonary vessels (cf pulmonary thromboembolism). This may occur almost instantaneously, as in near instant death following aircraft disasters.

2. The second phase develops as the onset of a chemical pneumonitis. Endothelial inflammation of small capillaries is caused by breakdown of embolic fat globules into toxic FFA, and due to the release of serotonin and histamine from embolism aggregated platelets. The ensuing increased capillary permeability results in the extravasation of proteinaceous fluid and even intra-alveolar haemorrhage.

From both mechanisms, hypoxia follows due to ventilation/perfusion mismatch, shunting, diffusion impairment, congestive atelectasis, decreased compliance and an increased dead space/tidal volume ratio. Type II pneumocytes are inactivated by FFA and surfactant production is diminished. Coagulation abnormalities may occur (i.e. disseminated intravascular coagulation), although infrequently. Cerebral effects often persist (at least temporarily) despite the correction of hypoxaemia and in the absence of direct cranial trauma. Renal function is rarely impaired. Hypovolaemic shock exacerbates right heart failure in FES.

Diagnosis

There is no pathognomonic sign or test during life, but a high index of suspicion is helpful in diagnosing FES in a patient who has respiratory and mental state changes 1-2 days following bone-trauma. One major and three minor/laboratory features in Table 1 may be highly suggestive of FES following trauma.

1. Clinical Features

There is usually a history of fracture of lower limb long bones, patient transport with insufficient fracture immobilization, or occasionally, arthroplasty and use of methylmethacrylate. A latent period of 24-48 hours frequently ensues before the onset of signs and symptoms, which may then progress rapidly. Dyspnoea and tachypnoea then develop, with cyanosis, cough and production of frothy bloodstained sputum less often seen. Initially, hypoxaemia is often present in FES with few respiratory signs. Petechial rash of the upper thoprax, axillae, neck, soft palate and conjunctiva occurs in 25-50% of cases. A mild to moderate fever of 38-39 °C is often present (in about 60%) during the acute phase, with an associated tachycardia. Mental changes are frequently seen in systemic embolization and may be the first clinical features observed. They include confusion, drowsiness, decerebrate signs, convulsions and coma. Expanding subdural/epidural collection after head injuries must be urgently excluded, usually by cranial CT scanning. Delirium tremens should also be considered.

Fat globules ("cotton wool spots") and petechiae are occasionally seen on retinal examination. A fall in cardiac output and increase in pulmonary vascular resistance has been shown to precede hypoxaemia in experimental fat embolism. Fulminant FES may have an onset in minutes to hours and is associated with hypotension, marked hypoxaemia, and often a poor prognosis.

2. Laboratory Tests

(a) *Arterial blood gases* - (with the patient breathing air) reveal a low PaO_2 (35-50 mmHg, 4.7-6.7 kPa), low $OaCO_2$ and respiratory alkalosis (from hyperventilation).

The appearance of a low PaO_2 usually precedes the onset of other clinical manifestations - the value of monitoring PaO_2 in patients at risk is thus obvious. There is an increase in the alveolar-arterial oxygen gradient and pulmonary shunt fraction.

(b) *Urine* - may contain fat globules (shown by the "sizzle" test using a platinum loop) as also may sputum (when stained with oil red O or Sudan III, IV), but neither test is reliable.

(c) *Coagulation/haematological* - Increased fibrin degradation products, thrombocytopenia and coagulation abnormalities (fat may release thromboplastin) may be detected during the acute phase of FES, but are not diagnostic. Bleeding problems are infrequently seen. A mild anaemia, sometimes with haemolytic features (detected by falling serum haptoglobin levels) is seen with FES. Intrapulmonary haemorrhage may be significant.

(d) *The cryostat test* - (in which clotted blood is frozen, sectioned and stained for fat) may be of assistance in detecting fat macroglobules microscopically (i.e. greater than 8 microm in diameter).

(e) *Blood chemistry* - Falling serial serum calcium levels may reflect the activity of circulating unbound FFA (forming soaps). Levels of both triglycerides and FFA are usually elevated in response to trauma and are not specific to FES.

(f) *Cerebrospinal fluid* - may stain positive for fat but is inconsistently seen in FES.

(g) *Chest radiography* - may often show diffuse "fluffy" opacification of lung fields bilaterally, peripherally and basally. Oedema may be sufficiently confluent to produce a "snowstorm" effect. Radiographic changes usually lag well behind deterioration of arterial oxygen tension. Effusions are not a feature of FES.

(h) *Electrocardiographic* - examination may reveal evidence of right heart strain in cases of fulminant FES.

(i) *Biopsy* - of kidneys and skin petechiae has revealed microinfarcts in association with fat macroglobules.

(j) *Enzyme tests* - have been used (i.e. serum tributyrinase, lipoprotein lipase, but not pancreatic lipase). Although levels may be elevated in FES after 5-8 days when the clinical signs are beginning to resolve, they do not aid in diagnosis.

Major trauma without FES can cause many of the above findings. Laboratory tests are often too insensitive and non specific to be clinically useful. *The diagnosis essentially remains a clinical one.* Differential diagnoses to be considered include pulmonary thromboembolism, cardiac or pulmonary contusion, septic shock, hypervolaemia, intracranial injury, aspiration pneumonitis, adult respiratory distress syndrome and transfusion reaction.

Repeated arterial blood gas analysis over 48 hours in these patients is the single most valuable guide to diagnosis and therapy.

Management

In the past, a number of different drugs and methods of treatment have been tried, some in large clinical trials, but with inconclusive results. These have included *ethyl alcohol* (a lipase inhibitor and emulsifying agent, used as an intravenous infusion or by nebulization to protect surfactant); *clofibrate* (to increase FFA metabolism); *dextran, heparin and aspirin* (to decrease platelet adhesiveness and promote microvascular blood flow); use of *increased fluids* (to decrease stress-associated catecholamine secretion and lipolysis); *fluid and salt restriction* (to decrease pulmonary extravascular water); systemic *corticosteroids* (to decrease permeability of damaged pulmonary capillaries, stabilise lysosome membranes and increase surfactant production); and *glucose and insulin* (as a nonlipid caloric source to avoid lipolysis). Heparin is also a lipoprotein lipace inducing agent, which hastens metabolism of intravascular lipids, but at the cost of forming more FFA which may further damage pulmonary capillary endothelium. Its use is controversial and probably best avoided. Trasylol (aprotinin) has not been found useful.

FES is a self-limiting disease and therapy is mostly suportive, with an emphasis on the maintenance of oxygen delivery to peripheral tissues. Management at present follows these guidelines:

1. Oxygen by Facemask

The arterial PaO_2 is checked at least daily for 5 days in patients at risk of FES. This test is the most sensitive index of FES effects on the lung and is gauging therapeutic responses. The supplemental flow of oxygen is altered accordingly. Continuous positive airway pressure (CPAP) via a facemask may alleviate the hypoxaemia further. If the arterial PaO_2 cannot be maintained above 60 mmHg (8.0 kPa) or if there is evidence of respiratory distress, hypercarbia and exhaustion, then mechanical ventilatory support is instituted.

2. Mechanical Ventilatory Support

Mechanical ventilation, preferably volume controlled, is along the usual lines. The inspired oxygen concentration should, if possible, be kept below 60%. Positive end expiratory pressure (PEEP) is sometimes required to obtained a satisfactory arterial PaO_2.

3. Adequate Circulating Volume

Adequate circulating volume must be ensured during the acute phase of FES following trauma (i.e. with colloid or red cell replacement). Untreated shock is associated with a poorer prognosis in FES. Blood and fluid loss at the fracture site is often underestimated. If clinical signs of FES develop and cardiovascular stability can be maintained, if necessary with inotrope support, then the judicious use of (a) fluid restriction, (b) diuretics, may improve blood oxygenation by decreasing pulmonary extravascular water. Valuable guidance as to the adequacy of therapy may be gained by monitoring central venous pressure and pulmonary capillary wedged pressure.

4. Aspirin, Dextran, Mini-dose Heparin

There is some evidence that these agents may be of limited benefit in decreasing platelet adhesiveness and formation of fibrin-fat emboli aggregates, but they are not used routinely. Their use may exacerbate bleed from sites of recent trauma.

5. Steroids

The use of steroids remain controversial. However, evidence of the beneficial effect of large doses of steroids (i.e. methylprednisolone 30 mg/kg/8 h for 3 doses), and lower doses of steroids has been produced both in the clinical setting and in experimental situations. Following steroid therapy, hypoxaemia may often be diminished. It is probably more effective if given prior to onset of the features of FES. Large clinical trials of steroid usage in FES therapy are few as yet.

Most cases of fat embolism recover merely with salt and water restriction, diuretics and oxygen. Resolution of clinical features usually occurs over 2-3 weeks. An early, and if necessary, aggressive approach is required for treating marked hypoxaemia, with oxygen, CPAP and mechanical ventilation. Other complications such as coma, coagulation problems and cardiac failure must be treated supportively as required. Death is more likely to occur due to respiratory failure than cerebral, renal or cardiac sequelae. Other than for the most fulminant cases, the prognosis is very good with no residual respiratory or cerebral impairment.

Prophylaxis of Fat Embolism

There is convincing evidence that the incidence of FES can be markedly reduced by adequate immobilization of fractures prior to patient transport and the early operative fixation of long bone fractures. The severity of the clinical syndrome may be reduced by prophylactic use of oxygen and avoidance of hypoxaemia. Repeated arterial blood gas analysis over the first 48 hours in these patients is the single most valuable guide to diagnosis and therapy.

Chapter 28: Acute Severe Asthma

D. V. Tuxen, T. E. Oh

Acute severe asthma can be defined as asthma which is life-threatening. It may arise in the absence of therapy or from inadequate or unsuccessful therapy, and is a medical emergency. Admission to an Intensive Care is mandatory.

Clinical Presentation

Acute severe asthma may arise from two clinical backgrounds:

1. *Acute severe asthma* usually occurs in patients whose lung function remains significantly abnormal in between episodes of clinically acute asthma. These patients often have minimal symptoms of asthma because of underperception of breathlessness, denial, and behaviour modification. As a result, they tend not to seek medical attention, and if they do, their asthma may be underestimated. Consequently, the asthma is often undertreated and poorly controlled. Acute severe attacks may devlop over hours to days, but the onset may appear precipitous, as significant symptoms may not arise until asthma is very severe. The response to treatment is variable, and may not be delayed. Thus respiratory fatigue and need for ventilatory support may arise before clinical improvement occurs.

2. *Hyperacute fulminating asthma* is less common and may occur in patients with normal or near normal lung function, but with a high level of bronchial reactivity. These patients may have a history of severe asthma or other evidence of high bronchial reactivity, such as marked diurnal variation of symptom or exercise-induced asthma. However, life-threatening asthma may arise de novo. The attack is usually rapid and may lead to respiratory insufficiency within hours of onset (even respiratory arrest within 30 min in the most severe form). Response to treatment is usually prompt and substantial. Respiratory support is often unnecessary or of short duration.

Asthma mortality and the requirement for mechanical ventilation is associated with these two patient categories. However, there is a spectrum of illness between the two groups, and many patients cannot be clearly categorized. Clinical precipitants include viral upper respiratory tract infections, allergens and irritants. No precipitants, however, can be identified in over 30% of patients.

Assessment of Severity

Clinical Features

The clinical features of asthma are well known and can be used to assess the severity of the attack.

1. Airflow Obstruction

Although expiratory *wheeze* is the hallmark of asthma, loudness of wheezing is not a good guide to airway obstruction. Very soft breath sounds or especially a "silent chest"

indicates grossly inadequate airflow ("locked lung syndrome"). *Pulmonary hyperinflation* occurs and usually becomes clinically apparent as asthma becomes more severe.

2. Ventilation - Perfusion Mismatch

Hypoxaemia and the requirement for increased minute ventilation are invariably present due to increased ventilation-perfusion mismatch. The degree of disturbances is roughly proportional to the severity of airflow obstruction.

Although *central cyanosis* can be clinically detected with as little as 1.5 g/dL deoxyhaemoglobin (which corresponds with a PaO_2 of 60 mmHg (8.0 kPa), hypoxaemia can remain undetected until it is severe. Thus hypoxaemia must be sought using arterial blood gases (ABGs) or pulse oximetry, or averted with oxygen therapy.

Tachycardia and arrhythmias may be present and are often associated with anxiety, increased work of breathing and sympathomimetic drugs. Nevertheless, a pulse rate over 130/min suggests severe hypoxaemia.

Increased minute ventilation requirements primarily results in *tachypnoea* because of limited capacity to increase tidal volume. As the severity of asthma worsens, ventilation requirement increases, tidal volume falls, and tachypnoea further increases. A reduction in tachypnoea without improvement in severe asthma indicates fatigue and impending respiratory collapse.

3. Increased Work of Breathing

The increased work of breathing due both to airflow obstruction and hyperinflation, results in an increased requirement for respiratory muscle force generation and use of *accessory respiratory muscles.* This results in *dyspnoea* and, as airflow obstruction worsens, *respiratory distress.* Assessment of the respiratory distress by both patient and experienced doctor can be used to judge the severity and the need for ventilatory assistance in some patients. However, other patients with severe airflow obstruction may have no symptoms and patient assessment of the response to treatment may be inaccurate. Increased work of breathing is also accompanied by assumption of an *upright posture* and *sweating,* both valuable indicators of severity of asthma.

The increased negative intrathoracic pressure generated during inspiration is also responsible for *pulsus paradoxus,* which is frequently present and may be a useful clinical indicator of airways obstruction. Note: pulsus paradoxus is an exaggeration of the normal slight fall in blood pressure and pulse volume on inspiration. A difference in systolic blood pressure between inspiration and expiration greater than 10 mmHg (1.3 kPa) indicates severe asthma. However, the degree of pulsus paradoxus does not necessarily correlate with the severity of the asthma, as it is also dependent on the capacity of the inspiratory muscles to generate negative intrathoracic pressure. If the inspiratory muscles are weak, or if their force generation is impaired by hyperinflation and fatigue, then pulsus paradoxus may be small or even diminish as airflow obstruction becomes more severe.

4. Ventilatory Failure

Ventilatory failure is manifested by a rising $PaCO_2$. This is usually accompanied by marked *distress, restlessness* and *anxiety.* As higher levels of $PaCO_2$ are reached, *flushing, further sweating,* and *bounding pulse* are seen, and may be accompanied by *exhaustion,* obtundation and a *depressed level of consciousness.* At this stage, ventilatory assistance is almost invariably required and should be instigated urgently.

Investigations

1. Arterial Blood Gases and Pulse Oximetry

Continutous pulse oximetry is desirable, and frequent blood gas estimations mandatory, until asthma is controlled. Hypoxaemia is almost invariably present in the patient with severe asthma breathing room air. Bronchodilators may transiently increase hypoxaemia by increasing ventilation perfusion mismatch (but should not be withheld for this reason).

Minute and alveolar ventilation are initially increased in an acute attack, leading to hypocarbia and respiratory alkalosis. As asthma severity and ventilation-perfusion mismatch worsens, the minute ventilation required to achieve the same alveolar ventilation increases. However, at the same time, it becomes increasingly difficult to meet this increased ventilatory requirement, and ventilation may diminish because of increased work of breathing, hyperinflation and fatigue. Thus a $PaCO_2$ rising towards normal represents clinical deterioration, rather than improvement, leading eventually to hypercarbia.

Acid-base status and serum bicarbonate levels may also be disturbed. Patients with poorly controlled asthma over several days may develop a mild non-anion gap metabolic acidosis (i.e. serum bicarbonate 22 ± mmol/L, presumably due to renal compensation for persisting hypocarbia). More severely ill asthmatics may develop lactic acidosis. The cause of this is uncertain but high doses of IV beta-2 agonists may contribute. The metabolic acidosis results in serum bicarbonate levels < 20 mmol/L and further increases ventilatory demand.

2. Ventilatory Function Tests

The asthmatic patient may be too breathless or distressed to perform even simple bedside lung function tests. However, forced vital capacity (FVC), one-second forced expiratory volume (FEV1) or peak expiratory flow rate (PEFR) are useful indices in assessing response to treatment, if they can be obtained. Usually, in severe asthma, FVC is less than one litre, FEV1 is less than 500 mL, and PEFR < 100 L/min. A ventilatory function test should be performed as soon as possible during an acute asthma attack and used to follow progress therafter.

3. Chest X-Ray

A chest X-ray is taken to exclude pneumothorax or mediastinal emphysema. The classical radiological features of acute severe asthma are a narrow central heart shadow,

flattened diaphragms, raised "bucket handle" ribs, and generalized hyperaeration. Any associated pulmonary parenchymal infection may be detected on the X-ray.

4. Electrocardiogram

Although the ECG is usually normal, in severe asthmatic attacks in young patients, ECG changes of right heart strain may occur (i.e. right axis deviation (RAD), P pulmonale, right bundle branch block (RBBB), S1Q3T3 pattern, and inverted T on anterior leads).

Diagnosis

The diagnosis of asthma is usually obvious. However, the combination of wheeze and dyspnoea are not infrequently caused by other illnesses. Left ventricular failure, aspiration pneumonia, upper airway obstruction, inhaled foreign body, and pulmonary embolism need to be remembered and excluded. Wheeze and dyspnoea arising in hospitalized patients not admitted with asthma, is more likely to be due to the above diagnoses than asthma.

Management

If acute asthma is judged to be severe, urgent treatment is warranted. Details about recent use of bronchodilators must be obtained with regard to type and dosage, especially aerosol sympathomimetics and slow-release theophylline preparation.

A. Primary Treatment

Initial pharmacotherapy of acute severe asthma should include some or all of the following:

1. Oxygen

Hypoxaemia should be promptly reversed with oxygen therapy. Although high inspired oxygen may lead to increased hypercarbia in patients with severe chronic airflow obstruction, this phenomenon is highly questionable in acute severe asthma and adequate oxygen therapy should not be withheld. The use of a pulse oximeter enables accurate titration of oxygen therapy to ensure SaO_2 of 96% or more. In a patient with severe chronic airways disease, inspired oxygen may be titrated to a lower SaO_2 without risking significant hypoxaemia.

Humidification of the inspired oxygen is desirable but poses practical problems. Heated water bath and gas-driven humidifiers produce droplets of a size which do not reach the small airways and may largerly settle on the oxygen face mask. Ultrasonic nebulizers are effective but are cumbersome and expensive. The cold aerosol may also increase airways resistance.

2. Nebulized Beta-2 Adrenergic Agents

Use of a nebulized beta-2 adrenergic agent remain first line bronchodilator therapy for severe asthma. Agents include salbutamol, terbutaline, fenoterol, and isprenaline.

(a) Salbutamol

Salbutamol acts rapidly and causes fewer side effects than the non-selective agents, but tremor and tachycardia may be problems. It may be nebulized using an oxygen mask and a disposable jet nebulizer unit (i.e. "Hudson", "Acorn", and "Inspiron"). The nebulizing dose is 1-2 mL of 0.5% solution every 4 hours. A minimum initial reservoir volume of 4 mL (with additional diluent) and an oxygen flow rate of 6-8 L/min are advocated to optimize nebulizer output. During the initial phases of severe asthma smaller, more frequent doses should be used (0.5-2 hourly intervals of 0.5-1 mL of 0.5% solution made up to 2-4 mL).

(b) Terbutaline, Fenoterol

Other beta-2 adrenergic agents, terbutaline and fenoterol, may be used as alternative. Their solution concentrations, 1.0% and 0.1% respectively, are such that similar volumes as for salbutamol are required. There is little difference in clinical effect compared with salbutamol.

(c) Isoprenaline

This may also be nebulized but is not preferred because of its non-selective beta action and hence increased propensity for tachycardia.

Metered aerosol bronchodilators generally are not completely effective in acute severe asthma because:

(i) patients with profound airways obstruction cannot inhale an aerosol effectively; and

(ii) have unusually repeatedly tried their own inhaler without much success before admission to hospital.

The inhalation technique of metered-dose inhalers is important. After exhalation, one puff of the inhaler is taken (either into the open mouth or with lips closed around the inhaler) just at the start of a slow, deep breath through the mouth. The breath is then held at full inspiration for 2-10 seconds. For those who cannot co-ordinate this manoeuvre, alternative methods of administration including a variety of tube spacers and dry powder inhaler (salbutamol "Rotacaps") are available.

As with nebulized bronchodilators, there are no major clinical differences between available aerosol beta-adrenergic inhalers. Although less than 10% of the dose is delivered to the airways, this is enough to be effective.

3. Ipatropium Bromide

Ipatropium bromide is an anticholinergic bronchodilator with no systemic atropine-like effects and no inhibition of mucociliary clearance. Although its bronchodilator action is not potent, it has good synergy with beta-2 agonists and has an accepted role in the treatment of asthma when used in this combination. It can be given in combination in the nebulizer solution, i.e. 1 mL 0.025% ipatropium with 1-2 mL 0.5% salbutamol.

4. Steroids

Although steroid therapy in acute severe asthma has been criticized, their use has become well established, with significant reductions in severity and hospital admission rates from short-term IV steroids. The exact mode of action is unknown but may be due to suppression of the inflammatory response, stabilization of mast cells, and potentiation of endogenous and exogenous catecholamines. The peak response is 6-12 hours after an IV injection, but the steroid effect may be seen as early as one hour.

The dosage is controversial. "High" doses (i.e. methylprednisolone 1 g every 6 hours) have been advocated in severe cases, but are probably not necessary. A suitable regimen is: hydrocortisone by continuous IV infusion of 0.5 mg/kg/h, or if given intermittently, 4 mg/kg every 3-4 hours. The duration of IV steroid therapy is usually several days but a single dose may be given. Intravenous steroids may be withdrawn abruptly if treatment is of short duration or replaced by a tapering dose of oral steroids (i.e. prednisolone commencing 40-60 mg/day in two divided doses) depending on the degree of lung recovery. Steroids should still be used in a pregnant woman with acute severe asthma. The risk of foetal anoxia from the asthma is far greater than any risk associated with correct use of steroids.

5. Aminophylline

Aminophylline contains 80% teophylline. The role of theophylline in asthma has been questioned and synergism with beta-2 agonists is debatable. In addition, IV aminophylline is associated with significant side effects which may outweigh benefits. Nevertheless, it remains an important treatment for those not responding to nebulizer treatment. Other potential effects of increasing cardiac output and diaphragmatic contractility may also be useful. If required, the IV loading dose of aminophylline is 5-6 mg/kg over 20-30 minutes. Aminophylline is continued as an infusion of 0.5 mg/kg/h but the doise is reduced in patients with cirrhosis, congestive heart failure, chronic obstructive lung disease, acute fevers, or receiving cimetidine, erythromycin or antiviral vaccines. The dose may need to be increased in young patients, smokers without chronic airflow obstruction, or regular alcohol consumers without liver disease.

Serum theophylline concentrations should be monitored with the therapeutic with the therapeutic range being 5-20 mg/L (30-110 micromol/L). Toxic effects include headache, nasue, vomiting, and restlessness, with life-threatening arrhythmias and convulsions at concentrations above 40 mg/L (200 micromol/L). Some 4% of adults are unable to tolerate even low serum levels. Initial serum levels correlate poorly with the history of the amount previously taken. Pharmacokinetic predictions of serum concentrations may optimize aminophylline infusions. Toxicity from duplicate prescribing (i.e. additional oral or rectal preparations) must be avoided.

Serum theophylline levels are used to monitor both the loading dose and the infusion rate. A serum level within 1-2 hours of the loading dose will identify inadequate or excessive loading, necessitating a further loading dose or temporary cessation of infusion. If load adjustment occurs, serum theophylline should be remeasured. Once the patient is optimally loaded, early steady state serum levels, usually 12 and 24 hours later, should be assayed. Levels should be monitored 24 hourly thereafter.

6. Intravenous Beta-2 Adrenergic Agent

Salbutamol may be given IV to patients with more severe asthma. It is given in a bolus dose of 100-300 microg, or a loading infusion up to 500 microg over one hour, followed by an infusion of 5-20 microg/min. The rate of infusion is limited by side effects, particularly tachycardia and tremor. Lactic acidosis, hyperglycaemia and hypokalaemia may be associated with IV salbutamol - the mechanisms are uncertain, but synergy with aminophylline may have a role. The acidosis may compound respiratory acidosis and distress and should be averted. Lactate levels respond within hours to reductions in the salbutamol infusion rate.

B. Other Treatment

Many other forms of therapy have been advocated for acute severe asthma, but they are either not advocated for routine use, nor always necessary or widely accepted.

1. Adrenaline

It is doubtful that adrenaline produces additional bronchial smooth muscle relaxation after full doses of beta-2 adrenergic agents. However, it may have equivalent treatment value without side effects and significant benefit may arise from its alpha-adrenergic actions of vasoconstriction and mucosal shrinkage, which may increase airway diameter beyond the effects of beta-2 adrenergic agents.

Adrenaline can be used by the subcutaneous route as 0.1 mg - 0.5 mg, repeated if necessary, 2 or 3 times at 30 minute intervals. Intravenous adrenaline may avert mechanical ventilation in very severe cases which have failed to respond to the above drugs. Since the patient is invariably hypoxaemic and hypercarbic, it has to be used with extreme caution, with mandatory continuous ECG monitoring. An IV test dose of 10 microg is given slowly over 3-5 minutes. If relief occurs promptly, a continuous infusion of 1-10 microg/min is started. The patient is gradually weaned off adrenaline when the acute attack is no longer life-threatening. Nebulized adrenaline is also effective and may be preferred to parenteral administration.

2. Other Drugs

Antihistamines have not been proven to be beneficial in acute severe asthma, even in patients whose asthma is known to be provoked by allergic exposure. Their anticholinergic effects may cause inspissation of secretions and worsening of airways obstruction. Mucolytic agents are also not considered to be effective.

Ketamine, a dissociative anaesthetic agent, has been reported to be useful in severe asthma. It decreases airways resistance, probably from increased circulating catecholamines from blocking their uptake into adrenergic nerve endings.

Halothane, droperidol, isoflurane and *enflurane* have also been reported to improve asthma but their benefit beyond optimal doses of standard bronchodilators is uncertain. *Calcium channelblockers* may have a role but this has not been clinically established.

3. Antibiotics

Acute asthmatic attacks are occasionally preceded by viral upper respiratory tract infections. Antibiotics are indicated only if there is clinical evidence of lower respiratory tract infection. However, antibiotics are not required in the majority of cases. Prophylactic use of antibiotics is not helpful.

4. Hydration

Patients with prolonged severe attacks may become dehydrated. Most patients on presentation are usually too breathless or exhausted to take fluids orally, and IV fluids are required. The role of fluids in decreasing sputum tenacity is uncertain. Usually a volume of 2.5-3.0 L/day is required and care must be taken against overload. Replacement of electrolytes, especially potassium, is given according to serum biochemical results.

5. Physiotherapy

During the initial phases of treatment, physiotherapy is ineffective, may be poorly tolerated, and may occasionally worsen airway narrowing. However, there is usually significant sputum plugs within the lungs and chest physiotherapy is an important adjunct to removal once sufficient bronchodilation has been achieved.

6. Sedation

There is no "safe" sedative in the management of the spontaneously breathing asthmatic. All sedative drugs carry a risk of central depression and increased morbidity and mortality. Patients with severe asthma should never be sedated unless being mechanically ventilated. Reassurance is important in reducing anxiety that may contribute to further increases in respiratory effort.

7. Non-Intravenous Medication

Althoug beta adrenergic agents are available for IM and subcutaneous use, and aminophylline is available in suppository form, these forms of administration have little or no role in the treatment of acute severe asthma.

C. Progress and Monitoring

Preventable morbidity and mortality may still occur usually as a result of a deterioration in asthma or patient status that is inadequately identified or treated. The major contributing factors are inadequate observation and measurement. Severe asthmatics should not be left unattended and attention is paid to the following.

1. *Close observation* - in an ICU or a specialized respiratory unit. This implies direct nursing observation and immediate abailability of medical staff.

2. *Regular measurement of asthma severity* - by a peak flow meter or portable spirometer. Clinical estimatation of asthma severity is not always reliable, whereas falls in

peak flow or FEV1 can provide early warning of deteriorating status. Once the patient is capable, measurements should be made 2-4 hourly during the initial phases of management.

3. *Regular measurement of blood gases and oxygenation status* are required.

4. *Close treatment monitoring* - this includes assessment of serum theophylline levels, frequency and dose of nebulised agents, and treatment side effects.

Mechanical Ventilation

Mechanical ventilation of patients with acute severe asthma may be life saving, but has a hgih risk of complications (especially barotrauma and hypotension) and an overall mortality of 13%. The most common single cause of death is cerebral hypoxia (Table 1) resulting from pre-hospital cardiorespiratory arrest. However, in the next 4 categories accounting for almost 50% of all deaths, mechanical ventilation potentially contributed to the deaths. Of all patients being ventilated for asthma, 14% developed pulmonary barotrauma (pneumothorax in 9% and pneumomediastinum or subcutaneous emphysema in 5%) and 38% developed hypotension.

Inadvertent pulmonary hyperinflation or gas trapping has been suggested as a major factor in ventilation associated complications. Following mechanical tidal expiration, normal or stiff lungs return to the passive relaxation volume of the respiratory system or the functional residual capacity (FRC). However, in severe asthma, there is significant prolongation of expiratory airflow and incomplete exhalation, prior to the next mechanical breath. Thus, a hypoventilating asthmatic initiated on mechanical ventilation, will undergo progressive hyperinflation. As lung volume increases, so too does airway calibre, thereby improving expiratory airflow, and proportionately less of each successive mechanical breath will be retained. Eventually, a steady state is reached in which there is sufficient hyperinflation for expiration of all the inspired volume. This process usually takes only 5-10 mechanically ventilated breaths.

Table 1. Cause of Death in Patients Requiring Mechanical Ventilation for Acute Severe Asthma

1. Cerebral ischaemia/hypoxia	26%
2. Hypotension	18
3. Sepsis with hypotension	10
4. Tension Pneumothorax	10
5. Technical complications with ventilator	10
6. Arrest post extubation	4
7. Inability to ventilate, hypoxia, perforated duodenal ulcer, peritonitis, aspiration, pneumonia	12
8. Not specified	8

The gas volume thus retained has been variously termed gas trapping, pulmonary hyperinflation, or increased end-expiratory lung volume. It may be measured during a period of apnoea long enough to allow complete exhalation of trapped gas (30-60 s). The pressure

exerted in the alveoli by this trapped gas at the end of tidal expiration, has been termed auto-PEEP, and may be measured by observing airway pressure during transient expiratory airway occlusion at the end of expiration.

Although hyperinflation may seem an appropriate physiological adaption to reduce airflow obstruction, the increased intrathoracic pressure can lead to two life-threatening problems - hypotension and barotrauma. The total lung volumes reached are within the capacity of a normal lung to expand safely, but there are large variations of airway calibre within the obstructed lung. This results in greater overexpansion of the more obstructed segments, with consequent risk of alveolar rupture.

The extent of hyperinflation is dependent on three prime factors:

1. The amount of air inspired - tidal volum (V_T).

2. The time allowed for expiration - expiratory time (T_E).

3. The severity of airflow obstruction.

Thus, an increase in minute ventilation, either by increasing V_T or increasing rate (reducing T_E) or both, is the biggest factor in increasing hyperventilation. At a constant minute ventilation, the ventilatory pattern giving the least hyperinflation is surprisingly one with a low V_T and a relatively higher rate. At any level of minute ventilation, hyperinflation will be reduced by increasing inspiratory flow rate, thereby allowing a longer T_E for a constant respiratory rate. However, the effects of increasing inspiratory flow on the distribution of ventilation within the lung remain controversial.

Ventilatory requirements to achieve normocarbia are highest during the initial phases of ventilatory support because of a high CO_2 production rate and ventilation: perfusion mismatch which reduces the efficiency of CO_2 excretion. The ventilatory requirements to normalize pH may be higher still if a metabolic acidosis is present. However, the ventilatory capacity of the lung is usually at its worst at this time, and attempts to normalize PCO_2 and pH will result in unsafe levels of hyperinflation in a significant number of patients.

Indications for Mechanical Ventilation

Ventilatory support should be avoided if possible, but initiated when there is significant risk of ventilatory collapse. The need for ventilatory support usually arises under two circumstances:

1. *Rapid fulminating asthma:* In this group airflow obstruction is so severe that only a very low level of minute ventilation is possible and pulmonary hyperinflation occurs to a degree where inspiratory muscles are ineffective, even in the absence of fatigue. These patients may present following a respiratory arrest or the need for ventilatory support arises shortly after presentation. Initial $PaCO_2$ levels are frequently > 80 mmHg (10.6 kPa) and may fall rapidly with prompt aggressive therapy, thereby averting the need for mechanical ventilation.

2. *Severe prolonged asthma:* In this group, although inspiratory muscles can sustain sufficient ventilation to initially achieve a $PaCO_2$ near or below normal, the increased work of breathing will ultimately lead to respiratory muscle fatigue. If therapy is inadequate or ineffective, these patients will manifest a rising $PaCO_2$ and will require ventilatory support at a much lower level of $PaCO_2$ than the first group.

Thus the decision to initiate ventilatory support should be based on the following considerations:

1. *Assessment of patient distress* is the single most important factor.

2. *State of treatment* - whether the patient has not yet received effective therapy or has failed to improve despite adequate therapy.

3. *Direction of change of $PaCO_2$* and clinical state. A single $PaCO_2$ measurement is the least important consideration.

Ventilatory Technique

1. *Initial ventilatory setting:* The initial stages of ventilatory support are the most critical and care must be taken to commence with a low level of minute ventilation (< 170 mL/kg/min or < 12 L/min in a 70 kg man). This should be achieved with a low tidal volume (< 10 mL/kg or 700 mL in a 70 kg man), a high inspiration flow rate (> 80 L/min), and rate adjusted to achieve the desired minute ventilation (< 20 breaths/min). Most asthmatics will be well oxygenated on 50% O_2 or less, unless there is another disease process present (such as pneumonia, aspiration or pulmonary oedema). This level of ventilation will usually result in hypercarbic acidosis, and patients will need sedation and often paralysis to disable attempts to increase their minute ventilation. Paralysis has the additional benefit of reducing CO_2 production. If significant hypotension occurs, minute ventilation should be further reduced by rate reduction and fluid loading given.

2. *Assessment of ventilation:* Once mechanical ventilation has bee initiated blood gases and the degree of pulmonary hyperinflation should be assessed. Hypercarbic acidosis should not be corrected by increasing ventilation without first assessing the degree of hyperinflation or its effects by any of these methods:

(a) Hypoventilation, maintaining peak ariway pressure < 50 cm water (4.9 kPa) until there is clinical improvement. This technique is simple and has proved effective. However, peak airway pressure is largely related to inspiratory flow rate and only representative of hyperinflation if inspiratory flow rate is constant and low.

(b) Measurement of plateau airway pressure during 0.5 sec end-inspiratory exhale occlusion - represents the alveolar pressure at the end of inspiration, which is directly proportional to the degree of hyperinflation, and should be maintained < 20 cm water (19,6 kPa). This corresponds with an approximate lung volume of 1.6 L above FRC, as most asthmatics have a near normal respiratory system compliance of approximately 80 mL/cm water.

(c) The end-expiratory exhale occlusion pressure (auto-PEEP) represents the alveolar pressure at the end of expiration and is proportional to the trapped gas volume. This value should be maintained < 12 cm water.

(d) Total exhaled volume (in steady state tidal ventilation of a paralysed patient) during a period of apnoea long enough (30-60 sec) for exhalation to be completed and the lungs to return to FRC. This volume should be maintained <20 mL/kg.

(e) A central venous catheter or an oesophageal ballon can both provide useful information on hyperinflation. The internal jugular route should be used, as the increased risk of pneumothorax from the subclavian route should be avoided. Pulmonary hyperinflation elevates intrathoracic and, hence, central venous and oesophageal pressures. The fall in these pressures and the increase in blood pressure during the period of apnoea, will indicate the degree of circulatory tamponade due to hyperinflation.

3. *Subsequent ventilatory adjustment:* If ventilatory assessment suggests a safe degree of hyperinflation, minute ventilation may either be maintained at that level or increased by increasing respiratory rate. If hyperinflation exceeds safe limits, then minute ventilation should be reduced *irrespective* of $PaCO_2$ or pH. A pH as low as 7.10 is generally well tolerated by patients with asthma. Even lower pHs may be corrected by IV sodium bicarbonate (100-200 mmol) given over 1-2 hours. During the initial stages of ventilation, the maximum safe level of ventilation is usually significantly less than the minute ventilation required for normocarbia. As asthma improves, both the ventilatory requirement for normocarbia reduces and the safe level of ventilation increases. When these two measurements are equal then the patient is ready for weaning and extubation.

PEEP and CPAP

The use of continuous positive airways pressure (CPAP) either via the endotracheal tube or by occlusive mask has recently been advocated to reduce the work of breathing in patients with COAD who are becoming fatigued. There is theoretical and some clinical evidence for benefit under these circumstances. However, this cannot be extrapolated to the use of PEEP during mechanical ventilation, as this has been shown to increase hyperinflation, airway and intrathoracic pressures, and depress the circulation.

Pneumothorax

There is a high incidence of pneumothorax in asthmatic patients undergoing mechanical ventilation which contributes to mortality. Once a pneumothorax has developed, airflow obstruction, which is worse during expiration, will favour continued gas loss through the ruptured alveolus rather than return of gas through the obstructed airway, thereby increasing the propensity for tension pneumothorax. A pneumothorax will reduce ventilation to the affected lung and increase ventilation to the unaffected lung. This in turn, increases hyperinflation of the unaffected lung, thus increasing the risk of developing bilateral pneumothoraces.

Prevention of pneumothoraces is by maintaining low levels of minute ventilation and hyperinflation, but awareness must be maintained, and careful safeguards instituted. A rise in

peak airway pressure during steady state ventilation is a valuable warning sign. Sedation and paralysis eliminate random patient respiratory movements which would normally cause transient rise in airway pressure.

Mortality

The reported overall mortality of asthma is significantly higher in Australia and New Zealand than in North America and has been increasing since the 1970s. While the majority deaths occurs prior to medical intervention, a significant proportion still occurs after medical help has been sought. The latter should be largely preventable.

Chapter 29: Pneumonias

D. V. Tuxen

Pneumonia remains a common and major cause of critical illness and death. Widespread use of immunosuppressive therapy and the autoimmune deficiency syndrome (AIDS) have caused an increase in pneumonia in these patient groups.

Normal Lung Defence

The respiratory system has complex defence mechanisms against airborne microbial invasion and aspiration of infected pharyngeal fluid - the major causes of pneumonias. The tortuous nature and moist lining of the upper airways causes air turbulence and impaction of most large airborne particles (over 10 microm in diameter) to airway wall. In addition to anti-microbial properties, upper airways are colonized by non-virulent resident flora which resist colonization by new pathogens. Upper airway secretions are ultimately swallowed or expectorated, and rarely enter the lower airway in the normal awake host. Entry of small volumes of oropharyngeal secretions into the lower respiratory tract during sleep is normal, and does not usually result in colonization. The sensory reflexes of the upper and lower airway and larynx provide prompt laryngeal closure, the gag reflex, coughing, and sneezing, which effectively eliminate large particulate or fluid matter.

The mucociliary blanket lining the trachea and airways filter out particles 2-10 microm in size. This mucous layer has both non-specific and specific anti-microbial defences, including detoxifying enzymes and locally secreted immunoglobulins. The mucociliary escalator also properls particles out of the tracheobronchial tree within hours of their entry. Phagocytosis and the lysosomal enzymes of alveolar macrophages and neutrophils, represent the final defence against particles under 2 microm in diameter which enter the alveoli. Lymphocytes provide additional defence against intracellular organisms by direct cytotoxic action and lymphokine release, which activates alveolar macrophages. Bloodborne pulmonary infection is uncommon, but is dealt with by blood-mediated defences similar to other non-aerated tissues.

Pathogenesis

Pneumonia may occur in a normal host with no apparent defect of lung defence mechanisms. However, more commonly, one or more abnormalities of host defence are

present (Table 1). Factors predisposing to pneumonia are frequently more important determinants of prognosis than the nature of the pneumonia. In general, a patient with an irreversibly impaired defence mechanism will have a worse prognosis and a higher risk of recurrence.

Table 1. Factors Predisposing to Pneumonia

Impaired upper airway defence

Depressed conscious level
Laryngeal dysfunction
Endotracheal intubation

Impaired coughing

Severe obstructive airways diseases
Respiratory muscle weakness
Thoracic or upper abdominal surgery
Laryngeal disorders
Reduced conscious state
Tracheostomy and endotracheal intubation

Impaired mucociliary blanket and escalator function

Airway diseases including chronic bronchitis, asthma, bronchiectasis
Smoking and atmospheric pollutants (SO_2, NO_2)
Hypercarbia
Prolonged high inspired O_2 concentration
Tracheostomy and endotracheal intubation
Suction and instrumentation trauma
Post viral and mycoplasma infection
Immotile cilia syndromes
Foreign bodies

Impaired alveolar phagocytic function

Smoking and atmospheric pollutants (SO_2, NO_2, ozone)
Alcoholism, starvation and debility
Steroid and immunosuppressive therapy
Hypothermia
Post viral infection
Uraemia, acidosis, acute hypoxia

Impaired immune defence

Gamma globulin deficiency (i.e. IgG deficiency)
Impaired cell mediated immunity (i.e. AIDS)

Aetiology

A broad range of pathogens may invade the lung. Although some pneumonias may be identified by a distinct clinical pattern or agent exposure, clinical findings are often non-specific. The majority of pneumonias are caused by pathogens commonly encountered in the environment. However, development of pneumonia is determined more by the host response than by exposure to the organism. Thus, a useful classification of likely aetiology is based on host status (Table 2). Nevertheless, a small number of less common pneumonias are determined primarily by unusual exposures rather than host status (Table 3). In the immunocompromised host, the range of pulmonary pathogens are much broader and includes numerous opportunists. Empirical therapy is thus difficult, as a number of antibiotics may be required, with a greater potential for side-effects. In a significant proportion of patients from all host groups, the causative organism is never isolated or determined.

Clinical Presentation

General Features

Pneumonia produces both systemic and respiratory manifestation. Common clinical findings include fever, sweats, rigors, cough, sputum production, pleuritic chest pain, dyspnoea, tachypnoea, tachycardia, pleural rub, rhonchi and signs of consolidation. Other organ systems may be involved depending on the type and severity of pneumonia. Hypotension from dehydration or high output circulatory failure may occur, and result in pre-renal renal failure or acute tubular necrosis. In addition, confusion, obtundation, abdominal pain, diarrhoea, paralytic ileus, disturbed liver function and electrolyte abnormalities may be present.

The presentation of pneumonia is traditionally divided into two clinical patterns.

1. *"Typical" pneumonia* is characterized by a sudden onset of an illness dominated by systemic features - high fever, sweats, rigors, pleuritic chest pain, and a "toxic" appearance. Dyspnoea and cyanosis may or may not initially be present, sputum is often initially absent. Chest X-ray shows a lobar or lobular opacity. The white cell count is usually markedly elevated and the causative organism is usually a typical bacterium, especially *Strep. pneumoniae, Klebsiella pneumoniae,* or *Haemophilus influenzae.*

2. *"Atypical" pneumonia* is characterized by a gradual onset of increasing respiratory illness, manifest by non-productive cough, dyspnoea and low grade fever. Clinical findings are often minimal. White cell count is often not elevated. Chest X-ray characteristically show a diffuse bilateral pulmonary infiltrate which appears worse than the clinical illness. Causative organisms are usually atypical and include *Mycoplasma pneumoniae, respiratory viruses, Legionella pneumophila, Chlamydia psittaci* and *Coxiella burneti.*

These two clinical groups may guide initial investigation and selection of empirical antibiotics. However, many presentations do not fit clearly into one or other category, and when patients can be categorized, correlation with characteristic causative organisms is far

from absolute. Other clinical patterns which typify a causative group of organisms can also be identified.

1. *Bronchopneumonia* in a patient with underlying chronic obstructive airways disease, is characterized by cough productive of purulent sputum, increasing dyspnoea, cyanosis and a patchy pulmonary infiltrate on chest X-ray.

2. *Viral pneumonia* is characterized by an upper respiratory prodrome and a rapid severe respiratory illness, with diffuse bilateral chest X-ray changes.

3. *Anaerobic pneumonia* is characterized by chronic cough, foul sputum, low grade fever, and cavitation on chest X-ray.

Specific Pneumonias

1. Pneumococcal Pneumonia

This pneumonia may occur in a normal host, but more commonly is associated with a host defence abnormality. Predisposing factors include cold exposure, viral upper respiratory infection, smoking, anaesthesia, underlying lung disease, debilitating illness, gamma globulin deficiency, immunosuppressive drugs and AIDS. Asymptomatic *Strep. pneumonia* is found in the nasopharynx of 20-40% of the population. Hence, isolation of the organism from sputum does not necessarily conclude its pathogenicity. Classical pneumococcal pneumonia occurs with a "typical" clinical pattern and a lobar or lobular consolidation. However, "atypical" clinical patterns and a diffuse radiological pattern may occur. The more severe forms may be complicated by septic shock, adult respiratory distress syndrome (ARDS), renal failure, disseminated intravascular coagulation (DIC), disturbed liver function, acute brain syndrome, and meningismus, and may be rapidly fatal despite prompt treatment with penicillin.

2. Klebsiella Pneumonia

This pneumonia is much less common, and usually occurs in male chronic alcoholics or patients suffering from other chronic debilitating diseases. Upper lobes are more commonly affected and the expanded nature of the consolidated lobe often causes the fissure to bulge. The pneumonia may be complicated by abscess formation, cavitation and empyema.

3. Mycoplasma Pneumonia

This type of pneumonia is associated with outbreaks in military barracks and institutions, and minor epidemics occurring every 4-5 years. It is the disease on which the description of primary atypical pneumonia was based. Severe cases may have associated haemolytic anaemia with renal failure, meningism, arthritis, rashes, and pulmonary embolism. Chest X-ray changes are most commonly diffuse but may be segmental or even lobar.

4. Legionella Pneumonia

This infection occurs sporadically or in outbreaks, due to inhaling contaminated water that has been aerosolized, usually by an air conditioner. Severity may vary, with a wide range of clinical manifestations. Patients may suffer malaise, high fever, rigors, and cough which is initially non-productive, but later produces mucopurulent sputum with occasional mild haemoptysis. Dyspnoea and pleuritic chest pain are less common features. Headache, nausea, vomiting, diarrhoea, abdominal pain, renal failure and electrolyte disturbances commonly occur. Chest X-ray changes are usually bilateral and extensive. There is a high mortality (approximately 15%). The disease has a predilection for hosts with serious underlying lung or systemic disease, and mortality in this group may be up to 50%.

5. Pneumocystis Pneumonia

This pneumonia occurs almost exclusively in patients with depressed immunity, especially those with AIDS, lymphoma, leukaemia, immunosuppressive therapy and chronic renal failure. The onset is usually insidious with low grade fever, dyspnoea, dry cough, and cyanosis. Early in the disease, malaise and dry cough may be the only features and the chest X-ray may appear normal. Later, the chest X-ray may show a diffuse bilateral pulmonary infiltrate of variable density.

6. Psittacosis

Psittacosis is primarily a disease of birds caused by *Chlamydia psittaci,* and infection is transmitted to man. Following an incubation period of 7-28 days, there is usually a sudden onset of high fever, rigors, and a dry irritating cough. Headache is a constant and severe feature, whereas dyspnoea may be mild or absent. Less commonly severe dyspnoea, pleuritic chest pain, pericarditis, upper respiratory symptoms, epistaxis, enlarged cervical nodes, myalgia, malaise and gastrointestinal (GIT) upset are present. Liver and spleen enlargement may be present and disturbed liver function may occur. A faint, macular rash (Horder's spots) may occur over the abdomen.

7. Enteric Gram Negative Pneumonia

This form of pneumonia most commonly occurs in hospitalized, debilitated or immobile patients, or in those with impaired laryngeal reflexes. The stomach is a major source of these organisms. Colonization with GIT flora and other organisms occurs with bowel stasis and antacid treatment. Common organisms are *E. coli, Proteus spp, Pseudomonas spp, Klebsiella spp,* as well as some gram positive organisms and fungi (i.e. *Staph. aureus, Strep. faecalis,* and candida). It is often clinically unclear whether pneumonia is actually present, or whether these organisms merely colonize the lower respiratory tract with the accompanying chest X-ray findings due to atelectasis caused by mechanical factors such as sputum retention. However, infection must be suspected, in view of recent reports of reduced rate of pneumonia, septicaemia and death, when these colonization patterns are prevented by prophylactic anti-microbial therapy. Established gram negative pneumonia may be complicated by cavitation. Causative organisms frequently co-exist with anaerobes, which are detected less often by routine culture.

8. Mycobacterial Pulmonary Infection

This chest infection is most commonly seen in patients with previous tuberculosis and apical scarring on chest X-ray, who have become alcoholics, debilitated, or immunosuppressed. The illness often has an insidious onset, with increased cough productive of purulent sputum, occasional haemoptysis, and sometimes, increasing dyspnoea. Typical chest X-ray appearance is one of an increasing upper lobe infiltrate with new cavitation. Sputum may show acid-fast bacilli, but their absence despite a typical clinical picture should not delay treatment, as culture confirmation may take up to 6 weeks.

Miliary tuberculosis is much less common. This usually occurs in a markedly immunosuppressed host who presents profoundly ill with high fever, dry cough and dyspnoea. Chest X-ray shows an extensive, bilateral, finely nodular infiltrate. The disease is rapdily progressive with a high mortality despite treatment. The most common organism is *Mycobacterium tuberculosis.* However, "atypical" mycobacteria are seen with increasing frequency in patients with AIDS.

9. Viral Pneumonia

Pneumonia may be caused by a variety of viruses including influenza A and B, parainfluenza, respiratory cyncitial virus (RSV), measles, varicella, cytomegalovirus, and occasionally, herpes simplex. Influenza viral pneumonia commonly occurs in epidemics. Patients with viral pneumonia often have a 1-2 day prodrome of an upper respiratory illness, and then become profoundly ill over a 24-48 hour period with dyspnoea, cyanosis, dry cough, and high fever. Ches X-ray shows a diffuse bilateral pulmonary infiltrate.

10. Herpes Simplex and Cytomegalovirus

Herpes simples virus (HSV) was once thought to occur rarely in the lower respiratory tract. However, HSV infection in this site is now known to be common, but is not usually associated with pneumonia. It is associated with critical illness, although it does not, by itself, worsen outcome. Rarely, HSV pneumonia may occur in severely immunosuppressed hosts, but to confirm this diagnosis, HSV must be isolated from bronchoalveolar lavage, percutaneous lung aspirate, or lung biopsy (preferably with histological evidence). HSV pneumonia should not be diagnosed from the presence of the virus in lower respiratory secretion alone.

Cytomegalovirus (CMV) is activaed less commonly in critical illness, and more commonly causes pneumonia. However, as with HSV, the presence of CMV in lower respiratory secretions is not conclusive of pneumonia, and other pathogens (i.e. pneumocystis) may be responsible.

Differential Diagnosis

A number of non infective pulmonary processes may mimic either focal or diffuse pneumonia. Respiratory illness resembling pneumonia with a focal chest X-ray change may be caused by infiltrating carcinoma, pulmonary infarct, or mechanical airway occlusion by tumour, foreign body or sputum plug. Airway occlusion is commonly duplicated by secondary

lower respiratory infection. Diffuse lung disease mimicking pneumonia may be caused by lymphangitis carcinomatosa, drug reaction, left ventricular failure, extrinsic allergic alveolitis, intrinsic alveolitis, or any other inflammatory or autoimmune lung disease. It is important to investigate a "typical" pneumonia which has failed to resolve with antibiotics, or an "atypical" pneumonia.

Diagnosis

Microbiological Diagnosis

1. Expectorated Sputum

Gram stain and culture of expectorated sputum is the traditional first line microbiological investigation. Unfortunately, it is also notoriously unreliable, with a specificity of approximately 50% and a sensitivity considerably lower. False negative cultures may be due to inadequate sampling (inadequate lower respiratory content), or organisms which cannot be seen on microscopy or cultured. False positives may occur if non-pathogenic colonizers are also present, or if the sample is contaminated with upper respiratory flora.

Microscopy and gram stain evaluation is more important than the culture result. The presence of a high white cell count and a low squamous cell count suggests a high lower respiratory and low oral secretion content. These findings help to validate the sputum sample. A gram stain showing large quantities of a single organism is more likely to yield a causative pathogen than one showing small quantities or a mixture of organisms (even though both sample types may culture the same organism). Positive cultures from sputum showing a high squamous cell content or mixed flora on gram stain, should not be regarded as significant.

2. Nasopharyngeal Aspiration

This procedure aims to obtain pharyngeal cells which may contain pathogenic viruses. This should be performed when viral pneumonia is suspected, and the sample should be subjected to viral culture and immunofluorescent antigen detection for influenza A and B, parainfluenza, measles, varicella, adenovirus, RSV, HSV, and CMV.

3. Lower Respiratory Tract Samples

Secretions may be obtained directly from the lower respiratory tract by suction catheter through an endotracheal tube, bronchoscopy aspiration and bronchoalveolar lavage, or transtracheal aspiration.

(a) *Suction catheter samples* are routinely obtained if an endotracheal tube is required for ventilatory or airway management. This provides a better quality sample than expectorated sputum. Suction catheters will usually traverse and obtrain secretions from the trachea, right main and right lower lobe bronchus. Curved tip suction catheters can be used to enter the left lower lobe.

(b) *Bronchoscopic aspiration* may be used in either the intubated or unintubated patient. Bronchoscopy allows visualization and aspiration of secretions from any pulmonary

subsegment. When used via an endotracheal tube, lower airway aspiration samples have little advantage over blind endotracheal suctioning, despite control over the area of aspiration. When used without an endotracheal tube, lower respiratory samples are reliably obtained. However, the bronchoscope (and hence the suctioning device) can become contaminated with upper respiratory flora during insertion. The use of protected brushes greatly reduces, but does not eliminate, this problem.

(c) *Bronchoalveolar lavage* is a fibreoptic bronchoscopic technique which obtains fluid with alveolar contents. The procedure involves wedging the bronchoscope tip in an infected pulmonary subsegment, and injecting normal saline in volumes up to 200 mL. Although such samples may still be contaminated by upper and lower respiratory organisms, they allow identification of causative organisms present in the alveoli but not in the airways. This technique has few complications, reduces the false negative rate, and should be used in all bronchoscopies performed for diagnosis of pneumonia.

The disadvantages of fibreoptic bronchoscopy are that:

(i) it is labour intensive;

(ii) it cannot always be performed before the commencement of therapy; and

(iii) it may seriously compromise a patient with severe hypoxia or incipient ventilatory failure.

(d) *Transtracheal aspiration* allows lower respiratory secretions to be obtained without traversing the upper airway. This consists of the introduction of a percutaneous needle or cannula through the cricothyroid membrane and subsequent sample aspiration. Complication include bleeding, subcutaneous emphysema, respiratory discomfort and distressing cough. Some reports have shown such samples to be more sensitive and specific than bronchoscopic aspirates. However, it is seldom practised, although commonly recommended.

4. Pleural Tap

A pleural tap is performed if a pleural effusion is present, especially if infected fluid or empyema is suspected. The majority of pleural effusions are sympathetic and free of organisms, but the causative organism may enter pleural fluid, and useful diagnostic information may be obtained. Empyema from rupture of an abscess or cavitating lesion, or from infected pleural fluid, must be diagnosed by pleural tap, as intercostal or formal surgical drainage is usually required.

5. Percutaneous Lung Aspiration

Direct lung aspiration provides access to alveolar fluid without airway contamination. Reported diagnostic yield has been variable (20-80%), being over 60% in the largest series.

Of the positive aspirates, 30% were accompanied by negative sputum culture, and 40% were accompanied by a false positive sputum culture. The procedure is complicated by a low rate of haemoptysis and pneumothorax, for which intercostal drainage is rarely required.

Occasional deaths have been reported in high risk patients in whom the value of the procedure was uncertain. Although bronchoscopy is used more commonly, this technique appears safe and effective, with high yields and minimal false positives. It should be considered if a more invasive diagnostic technique is desired in a non-ventilated patient, and if bronchoscopy is contraindicated or unavailable, or if sampling from a specific parenchymal lesion remote from the major airways is desired.

6. Lung Biopsy

Lung biopsy may be performed after other diagnostic attempts have been negative, treatment has been unsuccessful, or when histology is desired (i.e. suspected malignant, granulomatous, or inflammatory lung disease).

(a) *Transbronchial lung biopsy* may be performed via a fibreoptic bronchoscope. This may yield diagnostic histology or culture, which will then avoid the need for open lung biopsy. However, its positive culture rate is not significantly greater than bronchoalveolar lavage. It carries a small but distinct risk of haemoptysis and pneumothorax, and the small sample size makes lung histology difficult. It should be used in relatively well patients where a non-pneumonic process is equally suspected, and should be avoided in those being mechanically ventilated or with incipient respiratory failure.

(b) *Open lung biopsy* is the most invasive diagnostic procedure, requiring general anaesthesia and mini-thoracotomy. The risk of haemoptysis and pneumothorax is less than with transbronchial biopsy. Sample size is seldom inadequate, and the diagnostic yield is significantly higher. It is the procedure of choice in ventilated patient, and those critically ill who require urgent diagnosis and confirmation. It may also be undertaken after failed transbronchial biopsy. Information from lung biopsy will not commonly lead to new treatment, but will often allow cessation of unnecessary and potentially toxic therapy.

All biopsy samples should be subjected to special investigations. These include stain and culture for *Legionella spp.* and *Mycobacteria spp*, stain for *Pneumocystis spp.* and *Cryptococcus spp,* antigen detection using immunofluorescent antibodies (i.e. HSV, CMV, *Legionella,* influenza A and B, parainfluenza), and viral culture. Cytological examination can reveal viral intranuclear inclusion bodies which may be characteristic, i.e. HSV. Electron microscopy may also be useful in identifying viral infection.

7. Non-Pulmonary Microbiological Diagnosis

(a) *Blood cultures* may be positive in up to 30% of patients with severe bacterial pneumonia. If the patient has recently received beta-lactam antibiotics, blood culture bottles containing penicillinase should be used. Whereas sputum or a lower respiratory samples may contain false positives, a positive blood culture is far more specific.

(b) Cold agglutinins are positive in up to 70% of patients with Mycoplasma pneumonia, an organism which cannot be seen on microscopy and is difficult to culture. Cold agglutinins may be negative early in the course of the disease. The chance of a positive test

increases with disease severity. Specificity is limited, as cold agglutinins may also be seen with psittacosis, Q fever, *Legionella* and respiratory viruses.

(c) *Serum antibody titres* may be detected for a number of pathogens. A rising titre over a two week interval may provide a retrospective diagnosis. These include *Legionella, Mycoplasma,* respiratory viruses, *psittacosis* and Q fever.

Non Microbiological Findings

1. Chest X-ray

The hallmark of pneumonia is a lung field opacity on chest X-ray. Occasionally, with early opportunistic infection in an immunocompromised host (i.e. early *Pneumocystis carinii* pneumonia in a patient suffering from AIDS), the chest X-ray may appear normal.

The radiological pattern may provide valuable clues to the diagnosis. Lobar consolidation is most commonly caused by pneumococcus. An upper lobe pneumonia with a downward bulging fissure may be a klebsiella pneumonia. Upper lobe cavitation may be tuberculosis, whereas cavitation elsewhere may suggest staphylococcal pneumonia or infection complicating airway occlusion by a foreign body or tumour. A nodular pattern may be a fungal infection or miliary tuberculosis. Diffuse pulmonary infiltration suggests an "atypical" pneumonia, or ARDS complicating a severe bacterial pneumonia. Other complications of pneumonia such as pleural effusion, empyema, lobar or segmental collapse, pneumothorax, or abscess formation may also be seen on chest X-ray.

2. Blood Gases and Pulse Oximetry

Arterial blood gases should always be estimated once pneumonia is diagnosed. Characteristic findings are hypoxia and a normal or low $PaCO_2$. A rising $PaCO_2$ with respiratory acidosis is usually accompanied by respiratory distress, and represents incipient respiratory failure. Metabolic acidosis may also occur with severe pneumonia complicated by shock. Pulse oximetry provides immediate assessment of oxygenation and response from inspired oxygen. It can be used to follow patient progress and reduce, although not eliminate, the number of blood gas assessments required.

3. Full Blood Examination

A leukocytosis with a shift to the left with toxic granulocyte changes are the most common finding and characteristic of bacterial pneumonia. A normal or low white cell count may be seen in overwhelming sepsis, "atypical" pneumonia (especially mycoplasma), respiratory viruses or psittacosis, or in an immunosuppressed host. Anaemia and thrombocytopenia may also be seen when the pneumonia is complicated by severe systemic sepsis.

4. Electrolytes and Liver Function Tests

Serum electrolytes, urea and creatinine should be performed routinely. Hyponatraemia and impaired renal function are features of legionella pneumonia. Disturbed liver function may occur in mycoplasma or legionella pneumonia.

5. Immune Status

Immunology tests should be performed in suspected immunodeficiency conditions. Neutrophil and lymphocyte counts are obtained from a differential white cell count. Protein electrophoresis and gamma globulin assay may reveal abnormalities or deficiencies. Helper lymphocyte (T4) count and human immunodeficiency virus (HIV) antibodies should be performed if AIDS is suspected. Although a depressed T4 lymphocyte count is suggestive of AIDS, it may also be reflected by acute illness, especially viral infection. Cell mediated immunity testing by intradermal injection of common antigens (including mantoux testing) may be useful in a well patient, but immunity is also commonly depressed by an acute illness.

6. Gallium Scan

Gallium scan is rarely indicated in pneumonia, but can be useful if pneumonia is suspected in an immunocompromised host with a relatively normal chest X-ray (i.e. a patient with AIDS). The gallium scan will show a markedly increased uptake in the lung fields if a pneumonic process is present.

7. Computerized Tomographic Scanning

CT scanning is also rarely indicated in pneumonia, but can be useful to diagnose abscess formation, cavitation, or pleural effusions, when plan X-rays are unclear. CT can also be used to guide needle aspiration of pulmonary lesions.

8. Ventilation:Perfusion Lung Scanning

Lung scanning has no primary role in the diagnosis of pneumonia, but is used to aid the diagnosis of pulmonary embolism. Pulmonary emboli can complicate a prolonged pneumonia and are easily overlooked when pre-existing respiratory disease is present.

Management

Pneumonia vary enormously in severity. The most severe forms may result in a moribund patient with multi-organ failure who requires immediate admission to an ICU.

Choice of Investigations

If a "typical" pneumonia where the likely cause is bacterial and empirical antibiotics are relatively non-toxic, initial investigations are usually limited to sputum and blood cultures or tracheobronchial aspiration if the patient is intubated. Bronchoalveolar lavage or percutaneous lung aspiration may be performed within the first 24 hours if there is particular

urgency for an accurate diagnosis. Invasive investigations are more usually instigated after 2-3 days if the patient has failed to respond to initial empirical antibiotic therapy.

Invasive investigations are more important in an "atypical" pneumonia or with an immunocompromised host, when the range of possible opportunistic pathogens and the potential for anti-microbial toxicity is greater. In some cases, such as pneumocystis pneumonia in a patient with AIDS, a confident clinical diagnosis may be made and empirical anti-microbial treatment commenced without extensive investigation. However, if the clinical pattern or association with a pathogen is not specific, bronchoalveolar lavage, percutaneous lung aspiration, or transbronchial biopsy should be performed prior to, or within 24 hours of commencing empirical antibiotics. An ill patient being ventilated or too critically ill to tolerate these procedures may require an open lung biopsy early in the course of management.

Antibiotics

Antibiotics should be commenced within hours of presentation after sputum and blood samples have been collected. When appropriate, invasive diagnostic procedures may be performed early. In the case of a non critically ill patient, antibiotics may be delayed until one of these procedures is performed.

1. Empirical Antibiotic Therapy

Empirical antibiotic therapy is started before the microbiological diagnosis is established, which may take days, and in many patients is never achieved. Such antibiotic therapy is based primarily on host status (Table 2) and on specific information available on presentation:

(a) Clinical pattern, i.e. "typical" versus "atypical" pneumonia.

(b) Chest X-ray appearance.

(c) Gram stain findings.

(d) Specific exposure risk, i.e. overseas travel or animal exposure (Table 3).

(e) Epidemic information, i.e. patients presenting during a mycoplasma epidemic.

2. Specific Antibiotic Therapy

A decision has to be made whether an isolated organism is pathogenic or contaminant before instituting changes in therapy. Once this and the organism's sensitivities have been determined, therapy should be revised to the most appropriate antibiotic(s). Other antibiotics should be then ceased. Care should be taken to avoid narrowing antibiotic cover to treat an unlikely pathogen, whilst a more likely organism which has not been isolated is untreated (i.e. an enteric gram negative organism cultured in the sputum of a patient with mycoplasma pneumonia).

General Supportive Measures

1. Oxygen Therapy

Oxygen should be administered by face mask in sufficient flow and concentration to achieve a PaO_2 80-100 mmHg (10.6-13.3 kPa) or SaO_2 95-96%. In patients with underlying severe obstructive airways disease, ventilatory status must be closely monitored and oxygen goals may need to be modified.

2. Humidification

Heated humidification or an ultrasonic water nebulizer should be applied if expectoration of tenacious secretions is difficult.

3. Physiotherapy

Chest physiotherapy is an important adjunct to clearing secretions. Encouragement of coughing and deep breathing are the most important aspects.

4. Posture

Patients are turned erect to make breathing easier. The patient may be transiently placed in head down on either side during physiotherapy, with care not to cause undue respiratory distress.

5. Fluids

Pulmonary capillary integrity is frequently disturbed in pneumonia, and the lung is more sensitive to fluid loading, especially with diffuse bilateral pneumonias. Patients should preferably be managed with mild fluid restriction. This is modified in circulatory or renal failure. Overhydration to reduce tenacity of secretions should not be attempted.

6. Inotropic Drugs

Inotropes are occasionally required in patients with severe pneumonia complicated by circulatory and pre-renal failure. The circulatory failure is usually associated with a high cardiac output and low systemic vascular resistance, unless therew is co-existent severe ischaemic heart disease. The usual inotropes of first choice are dopamine or dopamine plus adrenaline or noradrenaline.

7. Mechanical Ventilation

A small percentage of patients with severe pneumonia require mechanical ventilation. The usual indications for intubation and mechanical ventilation are:

(a) Hypoxaemia despite high flow 100% O_2 delivered by facemask.

(b) Ventilatory failure manifest by increasing respiratory distress, and/or increasing respiratory acidosis.

(c) Respiratory arrest.

(d) Sputum retention refractory to conservative management.

High inspired O_2 concentrations are usually required and reduced pulmonary compliance results in increased inflation pressures. Positive end expiratory pressures (PEEP) should be used to improve oxygenation and reduce the inspired oxygen to 50% or less if possible. Even when lobar pneumonia is present, there is often a useful response to PEEP without significant asymmetry of lung inflation. PEEP may need to be avoided or used with caution, when cavitation or a bronchopleural fistula is present. As in any lung disease with reduced pulmonary compliance, risk of barotrauma should be minimized by the use of low tidal volumes when high airway pressures are identified (especially the plateau airway pressure during 0.5 sec end-inspiratory occlusion).

Empyema

Heavily infected pleural fluid or empyema is not adequately treated by systemic antibiotics alone, and must be drained. Watery, non-viscid and non-loculated fluid may be adequately drained by a wide-bore intercostal catheter. However, thick and purulent fluid, or loculation may require formal thoracotomy.

Chapter 30: Aspiration Syndromes

D. V. Tuxen

Aspiration of fluid, with or without solids into the lower respiratory tract is a common and potentially serious problem. There is a high associated mortality rate (about 60%), depending on the volume and type of aspirate, although it is usually preventable.

Aetiology

Aspiration results from the simultaneous occurrence of two abnormalities:

1. presence of fluid (i.e. gastric contents or blood) or particulate matter in the pharynx; and

2. impaired laryngeal defence, allowing pharyngeal contents to enter the lung.

Table 1. Conditions with Aspiration Risks

Altered Conscious States

Cerebrovascular accidents
Head injuriesw
Epilepsy
General anaesthesia
Alcohol or drug overdose
Metabolic coma

Impaired cough and gag reflexes

Recent extubation of larynx
Motor or sensory bulbar disturbance
Elderly patients
Seriously ill patients

Passive regurgitation

Obstetric cases
Emergency surgery for bowel obstruction
Hiatus hernia
Oesophageal obstruction
Nasogastric tube
Raised intra-abdominal pressure by succinylcholine
Oesophagoscopy

Table 1 shows some conditions which predispose to aspiration of gastric contents. It is important to be aware of the risk of passive regurgitation, when there is either a depressed conscious state or impaired cough and gag reflexes. Wide bore nasogastric tubes prevent closure of the upper and lower oesophageal sphincter, and also interfere with coughing and clearing of the pharynx. They may thus predispose to aspiration. Endotracheal intubation is protective against large volume aspiration, but, by splinting the vocal cords and epiglottis open, allows small volumes of pharyngeal fluid to pass below the vocal cords and accumulate above the endotracheal tube cuff. Indirect evidence from bacterial isolation patterns and glucose testing of endotracheal aspirate, suggests that small amounts of this fluid enter the lung. Such micro-aspiration does not cause major lung injury, but is associated with microbial colonization of the lung which may be harmful.

Types of Aspiration

The most useful classification of the aspiration syndromes is based on the nature of the aspirate:

1. acid aspiration;

2. infected fluid aspiration;

3. inert fluid aspiration;

4. particulate aspiration; and

5. other substances.

Acid Aspiration

The most serious form of aspiration is that resulting from acidic gastric contents. Consequent severity of lung injury is dependent on the volume and pH of the aspirate. There is a reported 100% mortality in patients whose gastric pH was less than 1.8 at the time of aspiration, and 25% mortality in those with a pH between 1.8 and 2.5. Although aspiration of gastric contents with a pH above 2.5 is considered to be non-acid aspiration, it is now recognized that this can also produce a similar, though less severe, pulmonary injury that is pathologically distinct from aspiration of non-gastric neutral fluids.

Normal gastric contents are acidic and free of microbial contamination. Consequently, with aspiration occurring in a previously well non-hospitalized patient, the aspiration fluid itself will not infect the lungs. Although the process of aspiration may introduce oral flora into the lower respiratory tract with the gastric contents, initial cultures are often negative. Subsequent colonization of the lower respiratory tract by predominantly gastrointestinal (GIT) gram negative organisms commonly occurs. This pattern appears to conform to that of any critically ill patient without being specific to acid aspiration. The pathological role of this colonization is uncertain but may be significant.

Pathology: Damage occurs within minutes of acid aspiration. There is loss of alveolar-capillary integrity and exudation of fluid and protein into the alveoli and bronchi. Within a few hours, there is bronchial epithelial degeneration, destruction of type II alveolar cells, and a polymorphonuclear cell infiltration, which progresses to alveolar consolidation. Macroscopically, the lungs are heavy, oedematous and haemorrhagic. At 48 hours, hyaline membranes can be seen, and at 72 hours, there is a reduction in the acute inflammatory response, with proliferation of fibroblasts and regeneration of bronchial epithelium.

Clinical features: Mendelson's syndrome is the term used to describe the severe dyspnoea, cyanosis, asthma-like reaction, and shock in association with the chemical pneumonitis from aspiration of a large volume of gastric fluid with pH less than 2.5. Interestingly, the patients originally described by Mendelson did not conform to acid aspiration in illness severity or mortality, and were more probably non-acid aspiration. Hypoxia can occur within minutes and is accompanied by dyspnoea and wheeze. Exudation

of protein-rich fluid into the alveoli leads to pulmonary oedema and a fall in dynamic compliance. This is often accompanied by hypovolaemia and hypotension. Chest X-ray usually shows diffuse bilateral pulmonary infiltrates, more marked at the lung bases, and may be indistinguishable from adult respiratory distress syndrome (ARDS). The clinical course of patients with severe aspiration is characterized by severe pulmonary injury and complications including circulatory failure, multisystem organ failure, and sepsis. Mortality is high, 25-100% depending on the severity of the insult and the host status.

Infected Fluid Aspiration

Although normal gastric acid contents are organism free, this is not so during illness and with use of antacid medication. All critically ill patients will have bacteria isolated from their nasogastric aspirate within 4 days of commencing antacid therapy, and 30% will have candidiasis. Organisms isolated are dominated by gram negative bacteria and anaerobes normally found in the lower GIT. Similar patterns of colonization of gastric fluid have also been found in a variety of GIT disturbances, achlorhydria, and paralytic ileus from any cause.

In 50-80% of critically ill patients, spread of GIT organisms to the lower respiratory tract by micro-aspiration of gastric contents can be demonstrated. Factors facilitating the retrograde spread of gastric fluid in the critically ill patient are the abscence of normal peristaltic and sphincteric action (due to sedation, paralytic ileus, and the nasogastric tube), the recumbent posture, and the presence of an endotracheal tube. In addition, the oropharynx may become heavily colonized during illness or in patients with poor oral hygiene. Such oropharyngeal flora will commonly also colonize the stomach and be introduced into the lungs directly by micro-aspiration.

The pathogenic role of gastric bacteria has now been clearly shown. Studies using prophylactic antibiotics to reduce bacterial and fungal colonization have resulted in a reduced incidence of pneumonia, septicaemia and death. Macroscopic aspiration is less common, but when it occur in a previously ill or hospitalized patient, especially those with GIT dysfunction or antacid treatment, a heavy innoculum of pathogenic bacteria will occur into the lower respiratory tract. This may be followed by infection and necrotizing bacterial pneumonia may occur. The organisms found depend on the clinical background of the host. In non-hospitalized patients, anaerobic oral flora sensitive to penicillin dominate. However, in hospitalized patients, cultures are dominated by GIT gram negative aerobes and anaerobes, which require a more broad spectrum antibiotic cover (Table 2).

Table 2. Lung Colonization Patterns Following Aspiration

Previously well, Non-hospitalized

Predominant oral flora, anaerobes/aerobes = 10/1
Bacteroides melanogenicus
Fusobacterium nucleatum
Peptostreptococcus
Bacteroides fragilis, oralis
Microaerophilic streptococci
Pneumococcus

Previously unwell, Hospitalized, Antacid used

Predominant GIT organisms and opportunists
E. coli, Klebsiella
Pseudomonas Proteus
Other Enteric flora
Staph. aureus
Candida albicans
Anaerobes

The histological changes are similar to, although less severe than, those seen in acid aspiration, but alveolar cell necrosis and the initial polymorphonuclear infiltration are less marked. Subsequent pathology becomes that of lower respiratory tract infection and pneumonia. The clinical course of infected, non-acid aspiration depends on the volume of aspirate, the efficacy of antibiotics, and whether lower respiratory infection becomes established. Although, with major aspiration, the initial hypoxaemia may be as severe as that of acid aspiration, initial alveolar injury is not as great, and hypotension and a prolonged ARDS-like injury are less common. The lung injury may progress to gradual resolution; otherwise, a more severe, prolonged illness ensues if pneumonia develops.

Inert Fluid Aspiration

Aspiration of neutral fluids which are free of bacteria and particulate matter such as blood, activated charcoal, isotonic solutions, and fresh or salt water, produces minimal or only transient chemical injury to the lung. The severity of clinical illness depends primarily on the volume of aspirate. Although lung injury may be mild, the physical presence of fluid disrupts gas exchange and can result in dyspnoea, cyanosis, and profound hypoxia. Chest X-ray shows focal or diffuse bilateral pulmonary infiltrates, indistinguishable from other forms of liquid aspiration. The clinical course is usually one of rapid improvement over several days, concurrent with radiological clearing, with little or no long term sequelae.

Particulate Aspiration

Particulate matter, such as partly masticated meat and vegetable material, may be aspirated either directly from the pharynx, or from vomited gastric contents. Aspiration of bone, tooth or amalgam fragments may follow jaw trauma, and inorganic objects (i.e. beads,

laryngoscope globes, gravel, coins, etc) can be aspirated under specific circumstances. Large inhaled particles will cause obstruction of major airways. Irritative food particles (i.e. meat, vegetable and dairy products) will, after an initial neutrophilic response, produce a more slowly developing and widespread granulomatous reaction, with macrophages and giant cells appearing at 48 hours. At 72 hours, most of the reaction is mononuclear with numerous granulomata. Hyaline membranes do not form, and despite a fibroblastic response at 3-7 days, minimal fibrosis remains at 21 days.

The clinical features of particulate aspiration depend on the volume of aspirate, the size of the particles and their complications. Large particles lodging in the hypopharynx, larynx or trachea will cause acute upper airway obstruction. Particles obstructing large airways may cause persistent coughing, dyspnoea, and focal or generalized wheezing. Uncleared particles may give rise to secondary infection, necrotizing pneumonia, abscess formation and empyema. Chest X-ray will commonly show focal consolidation or collapse corresponding with the obstructed areas, and radio-opaque particles may be visible. Non-obstructing particulate aspiration resulting from fine food particles in neutral gastric fluid (i.e. after a meal) may cause a clinical and radiological picture similar to that of acid aspiration. However, the fluid shift from the intravascular space to the lungs occurs later (about 3-4 hours after aspiration), and is not as great. Nevertheless, hypoxia may be just as severe, and the mortality rate is similar to that of acid aspiration if large volumes are aspirated.

Aspiration of Other Substances

A large variety of other substances which are injurious to the lung may occasionally be aspirated. These include feeding solutions and other lipid containing liquids, volatile hydrocarbons, and noxious gases. Each has a distinct clinical pattern and may produce unique histopathological features such as those seen in lipoid pneumonia.

Clinical Features

Although the aspiration syndromes differ in severity, course and outcome, they have many clinical features in common.

Acute aspiration is typically manifested by a sudden onset of some or all of the following: cough, dyspnoea, wheeze, tachypnoea, stridor, crepitation, rhonchi, cyanosis, hypotension, tachycardia and fever. There may be a history of vomiting, or evidence of vomitus, other secretions, or blood in the mouth or adjacent areas. However, absence of vomitus or other secretions does not exclude the diagnosis. A risk factor predisposing to aspiration (Table 1) is usually evident.

Chronic recurrent aspiration is most commonly seen in patients with subtle abnormalities of bulbar function. It may present with an insidious deterioration of respiratory function, in association with intermittent symptoms including cough, dyspnoea, wheeze, crepitations and rhonchi. There may be a history of coughing or choking after food or fluid ingestion. Careful neurological examination may be required if the risk factor for aspiration is not obvious.

Diagnosis

Diagnosis involves ascertaining that aspiration has occurred and establishing its type.

Establishing Diagnosis

1. *A clinical trial* is the basis for an initial diagnosis, namely

(a) a deterioration in respiratory function,

(b) history or evidence of vomiting, or presence of aspiratable substances, and

(c) identification of a predisposing factor (Table 1).

2. *An endotracheal aspirate sample* can confirm the diagnosis if it is similar in appearance to nasogastric aspirate, if bilirubin can be detected using a reagent strip indicator (i.e. Ames Multistix or Bililabstix), or if food or other particulate matter can be identified.

3. *Bronchoscopy* can confirm the diagnosis by identifying particulate matter. Cytological examination of *bronchial washings* should be sent to identify vegetable or meat fibres.

4. *Chest X-ray* findings are non-specific and may not be evident for a few hours. However, absence of a pulmonary infiltrate thereafter, excludes a major aspiration injury. Bilateral diffuse shadowing is present in over 50% of cases, being extensive in severe acid aspiration. If focal changes are present, the regions most commonly affected are the right upper lobe in the supine patient, and the right middle and lower lobes in the sitting or semirecumbent patient.

5. *Laryngeal incompetence* may be detected in patients who are otherwise neurologically normal, by careful observation of the patient drinking a small amount of water, or by laryngoscopy or a barium swallow.

Establishing Type of Aspiration

1. Vomitus and/or nasogastric aspirate should be

(a) examined for the presence of particulate matter,

(b) tested for pH prior to any antacid administration, and

(c) gram stained and cultured.

2. An endotracheal aspirate sample should be gram stained and cultured.

3. Bronchoscopy may be required to determine the presence or extent of particulate aspiration and to remove aspirated particles.

Establishing Severity of Aspiration

Severity of aspiration is best assessed by the clinical features and the degree of hypoxia by blood gases or pulse oximetry.

Differential Diagnosis

If evidence of aspiration is not obvious or if subtle abnormalities of bulbar function are present, aspiration may be misdiagnosed as acute pulmonary oedema, asthma, sputum retention or ARDS. As a result, aspiration may not be appropriately treated, leaving the patient at risk of further aspiration. Care must be taken to exclude aspiration when the above diagnoses are considered.

Management

1. Immediate Measures

If the incident is observed, immediate measures to clear the tracheobronchial tree are indicated. The patient should be turned onto the right side, and tilted head downwards. This may localize the aspiration to the right side of the lungs and prevent further aspiration from occurring. Suction and oxygenation can then be applied. If the patient has a reduced level of consciousness or has inadequate airway protection or clearance, the trachea should be intubated and aspirated as quickly as possible. Although inhaled fluid quickly disperses, suction will clear any solid or semisolid material. If clinical and radiological signs of airway obstruction are present, bronchoscopy should be performed.

In the conscious patient with minimal respiratory distress, it is reasonable to rely on chest physiotherapy to clear the tracheobronchial tree. However, if significant respiratory distress is present, tracheal intubation and suction is indicated. In all patients following intubation, and in some patients not requiring intubation, a nasogastric tube should be inserted to empty the stomach and reduce the risk of further aspiration. Bronchial lavage is of doubtful value, as pulmonary epithelial damage occurs early and bronchial secretion quickly buffer any aspirated material.

2. Oxygen Therapy

A high inspired oxygen fraction (FIO_2) should be supplied, to esnure a safe PaO_2. Continuous pulse oximetry should be performed or arterial blood gases should be taken at regular intervals, to monitor lung function.

3. Mechanical Ventilatory Support

The indication for controlled ventilation are respiratory distress and failure to maintain satisfactory PaO_2 or $PaCO_2$ levels. Positive end expiratory pressure (PEEP) is often required where a high FIO_2 is necessary to maintain an adequate PaO_2.

4. Bronchodilator Therapy

In acid aspiration, bronchospasm may be severe. Although the efficacy of bronchodilators in this condition is not great, inhaled beta-2 adrenergic bronchodilators should be given. Aminophyline (IV 5-6 mg/kg/h as an infusion) may be added.

5. Cardiovascular Support

In severe acid aspiration, the outpouring of protein-rich fluid into the lungs cause severe hypotension, which is best treated with plasma (i.e. 5% stable plasma protein solution). In the severely ill, Swan-Ganz catheterization with maintenance of a relatively low pulmonary capillary wedge pressure may be useful. Inotropic support may be necessary. Adrenaline (1-10 microg/min) or dopamine (5-20 microg/kg/min) are usually effective. Cautious monitoring of fluid balance is necessary, and mild fluid restriction is indicated, after the circulation has been stabilized, especially while the patient requires mechanical ventilation. Diuretic therapy is indicated if pulmonary oedema is associated with an elevated pulmonary capilly wedge.

6. Bronchoscopy

Therapeutic bronchoscopy is indicated if there is:

(a) particulate aspiration; or

(b) focal pulmonary collapse (suggesting large airway obstruction); or

(c) foreign bodies are visible on chest X-ray.

Rigid bronchoscopy allows wide bore suctioning and access of large grasping instruments into the lower respiratory tract. It is usually the procedure of choice, especially for the removal of semi-solid material. Rigid bronchoscopy does, however, carry the inconvenience of requiring general anaesthesia and re-intubation. Also, because of its size and rigid nature, it has limited access to upper lobes and more peripheral airways. Flexible fibreoptic bronchoscopy may be performed under local anaesthesia, through an existing endotracheal tube. With a wide range of grasping instruments available, it may be the procedure of first choice for more peripheral airwat occlusion, especially those beyond direct vision and for solid foreign particles (i.e. tooth or amalgam fragments).

7. Antibiotics

The role of infection in aspiration is uncertain and the use of antibiotics debated. It is useful to consider lower airway colonization or infection in 4 categories.

(a) *Aspiration of oral flora.* This usually occurs in previously well, non-hospitalized patients (Table 2) and may be associated with acid, particulate or inert aspiration. It is dominated by penicillin sensitive anaerobes. However, the pathogenic role of these bacteria is doubtful, and there have been no studies showing clear benefit from the use of penicillin. Secondary airway colonization with bowel flor may follow depending on the severity and duration of illness.

(b) *Heavy micro-organisms innoculation due to infected fluid aspiration.* This usually occurs in previously unwell, hospitalized patients, especially those on antacid therapy. Although there have been no studies specific to this group, there is indirect evidence of the pathogenic role of aspirated bacteria and the benefit of antibiotics.

(c) *Secondary airwayl colonization of a lung already injured by aspiration.* Microbiological isolation patterns are not specific to aspiration but conform with those seen in any seriously ill patient. Several studies have shown no benefit from antibiotics following aspiration and many believe infection does not play a major pathogenic role. However, there have been no well controlled clinical studies in patients with aspiration, and more recent studies of critically ill patients without aspiration suggest benefit from antibiotics in controlling such secondary infection.

(d) *Secondary infection in obstructing particulate aspiration.* Primary therapeutic requirement remains relief of the obstructed airway and drainage of any infected fluid collections. However, the pathogenic role of bacteria in necrotising pneumonia and empyema is not debated.

As the role of infection remain uncertain, the role of antibiotics remains controversial with no clear evidence of benefit or lack thereof. Although an expectant approach is recommended by some authors many others recommend their use despite uncertainty about their efficacy. If prophylactic antibiotics are to be used, a rational approach should be based on the type of aspiration which has occurred, and the bacteria commonly associated (Table 2).

More serious and prolonged lung injury is associated with acid, infected and particulate aspirate, all of which have a risk of both primary and secondary lung infection, and the use of antibiotics can be justified. This will necessitate gram positive, gram negative, and anaerobe cover, and flucloxacillin, a third generation cephalosporin, with metronidazole or clindamycin for anaerobe cover will achieve this. Third generation cephalosporins are prefered to aminoglycosides in airway infections because of their improved penetration and activity in respiratory secretions.

An expectant approach without antibiotics may be taken with inert fluid aspiration where more prompt resolution without complications can be expected. Regular sputum cultures should be performed to detect the emergence of any pathogens and antibiotics commenced only if clinically indicated.

8. Corticosteroids

Although some studies using animal models have suggested benefit from very early administration of steroids, the majority of studies in both acid and non-acid aspiration have concluded no benefit and possible detriment in relation to septic complications. In non-acid aspiration of foodstuff, experimental evidence indicates that steroids are contra-indicated, as they interfere with the ability of fibroblasts to wall off foreign material. Most current opinion does not support their use in any form of aspiration.

Prevention

1. Posture

In any unconscious patient at risk, a head down, semi-prone position should be maintained until the patient is intubated with a cuffed endotracheal tube.

2. Suction

Efficient suction must be readily available whenever unconscious patients are being nursed, and the sucker should be at hand during intubation procedures.

3. Cricoid Pressure

During induction of anaesthesia for endotracheal intubation in a patient at risk, cricoid pressure may be lightly applied while the patient is still awake (provided there is adequate explanation), then firmly applied as soon as consciousness is lost. It is important to train staff in its effective and safe application during rapid sequence induction. Awake intubation techniques should always be considered when difficulty with intubation is anticipated.

4. Airway Protection

If patients are unable to protect their airway or spontaneously clear pharyngeal fluids, because of either a depressed level of consciousness or impaired bulbar function, endotracheal intubation should be undertaken. If the problem fails to resolve, then this will need to be replaced by a tracheostomy for long term protection.

5. Nasogastric Tube

Nasogastric tubes must be aspirated regularly (2-4 hours) and left on free drainage as necessary to prevent accumulation of gastric secretions. Fine-bore nasogastric feeding tubes which do not allow suctioning must not be used until gastric emptying is assured. Monitoring of pH with indicator paper identifies those patients at high gastric acid levels, and serves as a routine in the prevention of the stress ulceration syndrome (i.e. maintain pH above 4.)).

6. Antacid Therapy and H2 Receptor Antagonists

Antacid therapy is used in critically ill and peri-operative patients to reduce the risk of acute stress induced ulceration and to reduce the risk of acid aspiration. More recently, these principles have been questioned because of the effects of antacid on gastric colonisation with micro-organism. There are also potentially adverse effects of some antacids if aspirated. Magnesium trisilicate has been a favoured antacid in the peri-operative situation and Intensive Care. However, there is growing concern about its efficacy and safety considering its particulate nature. Particulate antacids may cause or aggravate apsiration pneumonitis in humans and dogs. Studies on dogs suggest that non-particulate antacids (i.e. 0.3 molar sodium citrate) are less damaging and as effective.

H2 receptor antagonists block gastric histamine receptors and reduce the volume of gastric juice by the volume of acid no longer secreted. Cimetidine 300 mg orally the evening before surgery, and repeated intramuscularly at least 1 hour preoperatively, has been shown to effectively reduce the volume of gastric contents and elevate the pH to safe levels during the perioperative period. Although effective intravenously, the duration of action is probably much shorter than the 4 hours reported for oral and intramuscular routes. Haemodynamic problems have been reported with the intravenous route and prolonged use may cause sedation and confusion, thrombocytopenia and inhibition of hepatic enzymes. Ranitidine 50 mg IV has a longer duration of action and may be given 8-12 hourly. It appears to be free of the side-effects encountered with cimetidine, and is thus prefered. Because of the microbial colonization induced by antacid therapy in critically ill patients, the use of antacids in combination with local and systemic anti-microbial therapy, or the use of the cyto-protective agent sucralfate instead of antacids, has been proposed. The effect of these agents on aspiration are not yet known.

7. Metoclopramide

This drug facilitates gastric emptying and also increases the tone of the lower oesophageal sphincter. However, the use of narcotics and atropine counteract these favourable effects.