Neonatal Mechanical Ventilation

The introduction of mechanical ventilation in the 1960s was one of the major new interventions in neonatology, which provided lifesaving support for infants with respiratory failure. Along with other technologic advancements, such as the administration of antepartum corticosteroids and replacement surfactant therapy, mechanical ventilation has led to improved neonatal survival, especially for preterm infants born less than 30 weeks gestation with immature lung function.

Although mechanical ventilation can be lifesaving, it may cause chronic lung injury resulting in bronchopulmonary dysplasia (BPD), a major complication of prematurity. As a result, continued efforts have been focused upon development of new technology, including the use of early continuous positive airway pressure (CPAP) in preterm infants at risk for neonatal respiratory distress syndrome (RDS) and strategies for neonatal ventilator care to maintain adequate gas exchange but minimize lung damage.

MECHANICAL VENTILATION

Mechanical ventilation is the medical term for artificial ventilation where mechanical means is used to assist or replace spontaneous breathing. This may involve a machine called a
ventilator or the breathing may be assisted by an Anesthesiologist, registered nurse, physician, physician assistant, respiratory therapist, paramedic, or other suitable person compressing a bag or set of bellows. Mechanical ventilation is termed “invasive” if it involves any instrument penetrating through the mouth (such as an endotracheal tube) or the skin (such as a tracheostomy tube). There are two main modes of mechanical ventilation within the two divisions: positive pressure ventilation, where air (or another gas mix) is pushed into the trachea, and negative pressure ventilation, where air is, in essence, sucked into the lungs.

Uses

Mechanical ventilation is indicated when the patient’s spontaneous ventilation is inadequate to maintain life. It is also indicated as prophylaxis for imminent collapse of other physiologic functions, or ineffective gas exchange in the lungs. Because mechanical ventilation serves only to provide assistance for breathing and does not cure a disease, the patient’s underlying condition should be correctable and should resolve over time. In addition, other factors must be taken into consideration because mechanical ventilation is not without its complications.

In general, mechanical ventilation is instituted to correct blood gases and reduce the work of breathing.

Common medical indications for use include:

- Acute lung injury (including ARDS, trauma)
- Apnea with respiratory arrest, including cases from intoxication
- Acute severe asthma, requiring intubation
- Acute on chronic respiratory acidosis most commonly with Chronic obstructive pulmonary disease (COPD) and obesity hypoventilation syndrome
- Acute respiratory acidosis with partial pressure of carbon dioxide (pCO2) > 50 mmHg and pH < 7.25, which may be due to paralysis of the diaphragm due to Guillain–Barré
syndrome, myasthenia gravis, motor neuron disease, spinal cord injury, or the effect of anaesthetic and muscle relaxant drugs

- Increased work of breathing as evidenced by significant tachypnea, retractions, and other physical signs of respiratory distress
- Hypoxemia with arterial partial pressure of oxygen \((\text{PaO}_2)\) < 55 mm Hg with supplemental fraction of inspired oxygen \((\text{FiO}_2) = 1.0\)
- Hypotension including sepsis, shock, congestive heart failure
- Neurological diseases such as muscular dystrophy and amyotrophic lateral sclerosis

**Associated risk**

Barotrauma — Pulmonary barotrauma is a well-known complication of positive-pressure mechanical ventilation. This includes pneumothorax, subcutaneous emphysema, pneumomediastinum, and pneumoperitoneum.

Ventilator-associated lung injury — Ventilator-associated lung injury (VALI) refers to acute lung injury that occurs during mechanical ventilation. It is clinically indistinguishable from acute lung injury or acute respiratory distress syndrome (ALI/ARDS).

Diaphragm — Controlled mechanical ventilation may lead to a rapid type of disuse atrophy involving the diaphragmatic muscle fibers, which can develop within the first day of mechanical ventilation.

This cause of atrophy in the diaphragm is also a cause of atrophy in all respiratory related muscles during controlled mechanical ventilation.

Motility of mucocilia in the airways — Positive pressure ventilation appears to impair mucociliary motility in the airways. Bronchial mucus transport was frequently impaired and associated with retention of secretions and pneumonia.
Complications

Mechanical ventilation is often a life-saving intervention, but carries potential complications including pneumothorax, airway injury, alveolar damage, and ventilator-associated pneumonia. Other complications include diaphragm atrophy, decreased cardiac output, and oxygen toxicity. One of the primary complications that presents in patients mechanically ventilated is acute lung injury (ALI)/acute respiratory distress syndrome (ARDS). ALI/ARDS are recognized as significant contributors to patient morbidity and mortality.

In many healthcare systems, prolonged ventilation as part of intensive care is a limited resource (in that there are only so many patients that can receive care at any given moment). It is used to support a single failing organ system (the lungs) and cannot reverse any underlying disease process (such as terminal cancer). For this reason, there can be (occasionally difficult) decisions to be made about whether it is suitable to commence someone on mechanical ventilation. Equally many ethical issues surround the decision to discontinue mechanical ventilation.

APPLICATION AND DURATION

It can be used as a short-term measure, for example during an operation or critical illness (often in the setting of an intensive-care unit). It may be used at home or in a nursing or rehabilitation institution if patients have chronic illnesses that require long-term ventilatory assistance. Due to the anatomy of the human pharynx, larynx, and esophagus and the circumstances for which ventilation is needed, additional measures are often required to secure the airway during positive-pressure ventilation in order to allow unimpeded passage of air into the trachea and avoid air passing into the esophagus and stomach. The common method is by insertion of a tube into the trachea: intubation, which provides a clear route for the air. This can be either an endotracheal tube, inserted through the natural openings of mouth or nose, or a
tracheostomy inserted through an artificial opening in the neck. In other circumstances simple airway manoeuvres, an oropharyngeal airway or laryngeal mask airway may be employed. If the patient is able to protect his/her own airway and non-invasive ventilation or negative-pressure ventilation is used then an airway adjunct may not be needed.

**Negative pressure machines**

![An iron lung](image)

The iron lung, also known as the Drinker and Shaw tank, was developed in 1929 and was one of the first negative-pressure machines used for long-term ventilation. It was refined and used in the 20th century largely as a result of the polio epidemic that struck the world in the 1940s. The machine is, in effect, a large elongated tank, which encases the patient up to the neck. The neck is sealed with a rubber gasket so that the patient’s face (and airway) are exposed to the room air.

While the exchange of oxygen and carbon dioxide between the bloodstream and the pulmonary airspace works by diffusion
and requires no external work, air must be moved into and out of the lungs to make it available to the gas exchange process. In spontaneous breathing, a negative pressure is created in the pleural cavity by the muscles of respiration, and the resulting gradient between the atmospheric pressure and the pressure inside the thorax generates a flow of air.

In the iron lung by means of a pump, the air is withdrawn mechanically to produce a vacuum inside the tank, thus creating negative pressure.

This negative pressure leads to expansion of the chest, which causes a decrease in intrapulmonary pressure, and increases flow of ambient air into the lungs.

As the vacuum is released, the pressure inside the tank equalizes to that of the ambient pressure, and the elastic coil of the chest and lungs leads to passive exhalation.

However, when the vacuum is created, the abdomen also expands along with the lung, cutting off venous flow back to the heart, leading to pooling of venous blood in the lower extremities. There are large portholes for nurse or home assistant access. The patients can talk and eat normally, and can see the world through a well-placed series of mirrors. Some could remain in these iron lungs for years at a time quite successfully.

Today, negative pressure mechanical ventilators are still in use, notably with the polio wing hospitals in England such as St Thomas’ Hospital in London and the John Radcliffe in Oxford.

The prominent device used is a smaller device known as the cuirass. The cuirass is a shell-like unit, creating negative pressure only to the chest using a combination of a fitting shell and a soft bladder. Its main use is in patients with neuromuscular disorders that have some residual muscular function.

However, it was prone to falling off and caused severe chafing and skin damage and was not used as a long-term device. In recent years this device has re-surfaced as a modern polycarbonate shell
with multiple seals and a high-pressure oscillation pump in order to carry out biphasic cuirass ventilation.

Positive pressure

The design of the modern positive-pressure ventilators were based mainly on technical developments by the military during World War II to supply oxygen to fighter pilots in high altitude.

Such ventilators replaced the iron lungs as safe endotracheal tubes with high-volume/low-pressure cuffs were developed.

The popularity of positive-pressure ventilators rose during the polio epidemic in the 1950s in Scandinavia and the United States and was the beginning of modern ventilation therapy.

Positive pressure through manual supply of 50% oxygen through a tracheostomy tube led to a reduced mortality rate among
patients with polio and respiratory paralysis. However, because of the sheer amount of man-power required for such manual intervention, mechanical positive-pressure ventilators became increasingly popular.

Positive-pressure ventilators work by increasing the patient’s airway pressure through an endotracheal or tracheostomy tube. The positive pressure allows air to flow into the airway until the ventilator breath is terminated.

Then, the airway pressure drops to zero, and the elastic recoil of the chest wall and lungs push the tidal volume — the breath-out through passive exhalation.

**Transairway pressure**

\[ P_{TA} = (P_{AO}) - (P_{ALV}) \]

- \( P_{TA} \) = Transairway pressure
- \( P_{AO} \) = Pressure at airway opening
- \( P_{ALV} \) = Pressure in alveoli

**Intermittent abdominal pressure ventilator**

Another type is the intermittent abdominal pressure ventilator that applies pressure externally via an inflated bladder, forcing exhalation, sometimes termed exsufflation. The first such apparatus was the Bragg-Paul Pulsator. The name of one such device, the Pneumobelt made by Puritan Bennett has to a degree become a generic name for the type.

**TYPES OF VENTILATORS**

Ventilators come in many different styles and method of giving a breath to sustain life. There are manual ventilators such as bag valve masks and anesthesia bags that require the users to hold the ventilator to the face or to an artificial airway and maintain breaths with their hands. Mechanical ventilators are ventilators not requiring operator effort and are typically computer-controlled or pneumatic-controlled.
Mechanical ventilators

Mechanical ventilators typically require power by a battery or a wall outlet (DC or AC) though some ventilators work on a pneumatic system not requiring power.

- Transport ventilators — These ventilators are small and more rugged, and can be powered pneumatically or via AC or DC power sources.
- Intensive-care ventilators — These ventilators are larger and usually run on AC power (though virtually all contain a battery to facilitate intra-facility transport and as a back-up in the event of a power failure). This style of ventilator often provides greater control of a wide variety of ventilation parameters (such as inspiratory rise time). Many ICU ventilators also incorporate graphics to provide visual feedback of each breath.
- Neonatal ventilators — Designed with the preterm neonate in mind, these are a specialized subset of ICU ventilators
that are designed to deliver the smaller, more precise volumes and pressures required to ventilate these patients.

• Positive airway pressure ventilators (PAP) — These ventilators are specifically designed for non-invasive ventilation. This includes ventilators for use at home for treatment of chronic conditions such as sleep apnea or COPD.

BREATH DELIVERY

Trigger

The trigger is what causes a breath to be delivered by a mechanical ventilator. Breaths may be triggered by a patient taking their own breath, a ventilator operator pressing a manual breath button, or by the ventilator based on the set breath rate and mode of ventilation.

Cycle

The cycle is what causes the breath to transition from the inspiratory phase to the exhalation phase. Breaths may be cycled by a mechanical ventilator when a set time has been reached, or when a preset flow or percentage of the maximum flow delivered during a breath is reached depending on the breath type and the settings. Breaths can also be cycled when an alarm condition such as a high pressure limit has been reached, which is a primary strategy in pressure regulated volume control.

Limit

Limit is how the breath is controlled. Breaths may be limited to a set maximum circuit pressure or a set maximum flow.

BREATH EXHALATION

Exhalation in mechanical ventilation is almost always completely passive. The ventilator’s expiratory valve is opened, and expiratory flow is allowed until the baseline pressure (PEEP)
is reached. Expiratory flow is determined by patient factors such as compliance and resistance.

MODES OF VENTILATION

Mechanical ventilation utilizes several separate systems for ventilation referred to as the mode. Modes come in many different delivery concepts but all modes fall into one of three categories; volume-cycled, pressure-cycled, spontaneously cycled. In general, the selection of which mode of mechanical ventilation to use for a given patient is based on the familiarity of clinicians with modes and the equipment availability at a particular institution.

Modification of settings

In adults when 100% Oxygen (O2) (1.00 \( \text{FiO}_2 \)) is used initially, it is easy to calculate the next \( \text{FiO}_2 \) to be used and easy to estimate the shunt fraction. The estimated shunt fraction refers to the amount of oxygen not being absorbed into the circulation. In normal physiology, gas exchange (oxygen/carbon dioxide) occurs at the level of the alveoli in the lungs. The existence of a shunt refers to any process that hinders this gas exchange, leading to wasted oxygen inspired and the flow of un-oxygenated blood back to the left heart (which ultimately supplies the rest of the body with unoxygenated blood).

When using 100% O2 (\( \text{FiO}_2 \) 1.00), the degree of shunting is estimated by subtracting the measured \( \text{PaO}_2 \) (from an arterial blood gas) from 700 mmHg. For each difference of 100 mmHg, the shunt is 5%. A shunt of more than 25% should prompt a search for the cause of this hypoxemia, such as mainstem intubation or pneumothorax, and should be treated accordingly. If such complications are not present, other causes must be sought after, and positive end-expiratory pressure (PEEP) should be used to treat this intrapulmonary shunt. Other such causes of a shunt include:

- Alveolar collapse from major atelectasis
• Alveolar collection of material other than gas, such as pus from pneumonia, water and protein from acute respiratory distress syndrome, water from congestive heart failure, or blood from haemorrhage

Weaning from mechanical ventilation

Timing of withdrawal from mechanical ventilation—also known as weaning—should be carefully considered. Patients should have their ventilation considered for withdrawal if they are able to support their own ventilation and oxygenation, and this should be assessed continuously.

There are several objective parameters to look for when considering withdrawal, but there are no specific criteria that generalizes to all patients.

The Rapid Shallow Breathing Index (RSBI, the ratio of respiratory frequency to tidal volume (f/VT), previously referred to as the “Tobin Index” after Dr. Martin Tobin of Loyola University Medical Center) is one of the best studied and most commonly used weaning predictors, with no other predictor having been shown to be superior.

It was described in a prospective cohort study of mechanically ventilated patients which found that a RSBI > 105 breaths/min/L was associated with weaning failure, while a RSBI < 105 breaths/min/L predicted weaning success with a sensitivity, specificity, positive predictive value and negative predictive value of 97%, 64%, 78%, 95% respectively.

RESPIRATORY MONITORING

One of the main reasons why a patient is admitted to an ICU is for delivery of mechanical ventilation. Monitoring a patient in mechanical ventilation has many clinical applications: Enhance understanding of pathophysiology, aid with diagnosis, guide patient management, avoid complications and assessment of trends.
Fig. Respiratory mechanics monitor

Most of modern ventilators have basic monitoring tools. There are also monitors that work independently of the ventilator, which allow to measure patients after the ventilator has been removed, such as a T tube test.

ARTIFICIAL AIRWAYS AS A CONNECTION TO THE VENTILATOR

There are various procedures and mechanical devices that provide protection against airway collapse, air leakage, and aspiration:

- Face mask — In resuscitation and for minor procedures under anaesthesia, a face mask is often sufficient to achieve a seal against air leakage. Airway patency of the unconscious patient is maintained either by manipulation of the jaw or by the use of nasopharyngeal or oropharyngeal airway. These are designed to provide a passage of air to the pharynx through the nose or mouth, respectively. Poorly fitted masks often cause nasal bridge ulcers, a problem for some patients. Face masks are also used for non-invasive ventilation in conscious patients. A full face mask does
not, however, provide protection against aspiration.

- **Tracheal intubation** is often performed for mechanical ventilation of hours to weeks duration. A tube is inserted through the nose (nasotracheal intubation) or mouth (orotracheal intubation) and advanced into the trachea. In most cases, tubes with inflatable cuffs are used for protection against leakage and aspiration. Intubation with a cuffed tube is thought to provide the best protection against aspiration. Tracheal tubes inevitably cause pain and coughing. Therefore, unless a patient is unconscious or anaesthetized for other reasons, sedative drugs are usually given to provide tolerance of the tube. Other disadvantages of tracheal intubation include damage to the mucosal lining of the nasopharynx or oropharynx and subglottic stenosis.

- **Supraglottic airway** — a supraglottic airway (SGA) is any airway device that is seated above and outside the trachea, as an alternative to endotracheal intubation. Most devices work via masks or cuffs that inflate to isolate the trachea for oxygen delivery. Newer devices feature esophageal ports for suctioning or ports for tube exchange to allow intubation. Supraglottic airways differ primarily from tracheal intubation in that they do not prevent aspiration. After the introduction of the laryngeal mask airway (LMA) in 1998, supraglottic airway devices have become mainstream in both elective and emergency anesthesia. There are many types of SGAs available including the Esophageal-tracheal Combitube (ETC), Laryngeal tube (LT), and the obsolete Esophageal obturator airway (EOA).

- **Cricothyrotomy** — Patients requiring emergency airway management, in whom tracheal intubation has been unsuccessful, may require an airway inserted through a surgical opening in the cricothyroid membrane. This is similar to a tracheostomy but a cricothyrotomy is reserved for emergency access.
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• **Tracheostomy** — When patients require mechanical ventilation for several weeks, a tracheostomy may provide the most suitable access to the trachea. A tracheostomy is a surgically created passage into the trachea. Tracheostomy tubes are well-tolerated and often do not necessitate any use of sedative drugs. Tracheostomy tubes may be inserted early during treatment in patients with pre-existing severe respiratory disease, or in any patient expected to be difficult to wean from mechanical ventilation, i.e., patients with little muscular reserve.

• **Mouthpiece** — Less common interface, does not provide protection against aspiration. There are lipseal mouthpieces with flanges to help hold them in place if patient is unable.

IRON LUNG

A negative pressure ventilator, often referred to colloquially as an iron lung, is a form of medical ventilator that enables a person to breathe when normal muscle control has been lost or the work of breathing exceeds the person’s ability. Examples of the device include both the Drinker respirator and the Both respirator. The negative form of pressure ventilation has been almost entirely superseded by positive pressure ventilation or biphasic cuirass ventilation.

**Method and use**

Humans, like most mammals, breathe by negative pressure breathing: the rib cage expands and the diaphragm contracts, expanding the chest cavity. This causes the pressure in the chest cavity to decrease, and the lungs expand to fill the space. This, in turn, causes the pressure of the air inside the lungs to decrease (it becomes negative, relative to the atmosphere), and air flows into the lungs from the atmosphere: inhalation. When the diaphragm relaxes, the reverse happens and the person exhales. If a person loses part or all of the ability to control the muscles involved, breathing becomes difficult or impossible.
The person using the iron lung is placed into the central chamber, a cylindrical steel drum. A door allowing the head and neck to remain free is then closed, forming a sealed, air-tight compartment enclosing the rest of the person’s body. Pumps that control airflow periodically decrease and increase the air pressure within the chamber, and particularly, on the chest. When the pressure is below that within the lungs, the lungs expand and atmospheric pressure pushes air from outside the chamber in via the person’s nose and airways to keep the lungs filled; when the pressure goes above that within the lungs, the reverse occurs, and air is expelled. In this manner, the iron lung mimics the physiological action of breathing: by periodically altering intrathoracic pressure, it causes air to flow in and out of the lungs. The iron lung is a form of non-invasive therapy.

Invention and early use

In 1670, English scientist John Mayow came up with the idea of external negative pressure ventilation. Mayow built a model consisting of bellows and a bladder to pull in and expel air. The
first negative pressure ventilator was described by Scottish physician John Dalziel in 1832. Successful use of similar devices was described a few years later.

Fig. Iron lung from the 1950s in the Gütersloh Town Museum. In Germany, fewer than a dozen of these breathing machines are available to the public.

Early prototypes included a hand-operated bellows-driven “Spirophore” designed by Dr. Woillez of Paris (1876), and an airtight wooden box designed specifically for the treatment of polio by Dr. Stueart of South Africa (1918). Stueart’s box was sealed at the waist and shoulders with clay and powered by a motor-driven bellows. The first of these devices to be widely used however was developed by Drinker and Shaw in 1928. The iron lung, often referred to in the early days as the “Drinker respirator”, was invented by Philip Drinker (1894–1972) and Louis Agassiz Shaw, Jr., professors of industrial hygiene at the Harvard School of Public Health. The machine was powered by an electric motor with air pumps from two vacuum cleaners. The air pumps changed
the pressure inside a rectangular, airtight metal box, pulling air in and out of the lungs.

The first clinical use of the Drinker respirator on a human was on October 12, 1928, at the Boston Children’s Hospital. The subject was an eight-year-old girl who was nearly dead as a result of respiratory failure due to polio. Her dramatic recovery, within less than a minute of being placed in the chamber, helped popularize the new device.

Boston manufacturer Warren E. Collins began production of the iron lung that year. Although it was initially developed for the treatment of victims of coal gas poisoning, it was most famously used in the mid-20th century for the treatment of respiratory failure caused by poliomyelitis.

Danish physiologist August Krogh, upon returning to Copenhagen in 1931 from a visit to New York where he saw the Drinker machine in use, constructed the first Danish respirator designed for clinical purposes. Krogh’s device differed from Drinker’s in that its motor was powered by water from the city pipelines. Krogh also made an infant respirator version.

In 1931, John Haven Emerson (February 5, 1906 – February 4, 1997) introduced and improved upon a less expensive iron lung. The Emerson iron lung had a bed that could slide in and out of the cylinder as needed, and the tank had portal windows which allowed attendants to reach in and adjust limbs, sheets, or hot packs.

Drinker and Harvard University sued Emerson, claiming he had infringed on patent rights. Emerson defended himself by making the case that such lifesaving devices should be freely available to all. Emerson also demonstrated that every aspect of Drinker’s patents had been published or used by others at earlier times. Since an invention must be novel to be patentable, prior publication/use of the invention meant it was not novel and therefore unpatentable. Emerson won the case, and Drinker’s patents were declared invalid.
The United Kingdom’s first iron lung was designed in 1933 by Robert Henderson, an Aberdeen doctor. Henderson had seen a demonstration of the Drinker respirator in the early 1930s, and built a device of his own upon his return to Scotland. Four weeks after its construction, the Henderson respirator was used to save the life of a 10-year-old boy from New Deer, Aberdeenshire, who was suffering from poliomyelitis. Despite this success, Henderson was reprimanded for secretly using hospital facilities to build the machine.

**Both respirator**

Fig. A Both cabinet respirator being used to treat a patient at the 110th Australian Military Hospital in 1943

The Both respirator, a negative pressure ventilator, was invented in 1937 when Australia’s epidemic of poliomyelitis created an immediate need for more ventilating machines to compensate for respiratory paralysis. Although the Drinker model was effective and saved lives, its widespread use was hindered by the fact that the machines were very large, heavy (about 102 kg), bulky, and expensive. In the US, an adult machine cost about $2000 in 1930, and £2000 delivered Melbourne in 1936. The cost in Europe in the mid-1950s was around £1500. Consequently, there were few of the
Drinker devices in Australia and Europe. The South Australia Health Department asked Adelaide brothers Edward and Don Both to create an inexpensive “iron lung”. Biomedical engineer Edward Both designed and developed a cabinet respirator made of plywood that worked similarly as the Drinker device, with the addition of a bi-valved design which allowed temporary access to the patient’s body. Far cheaper to make (only £100) than the Drinker machine, the Both Respirator also weighed less and could be constructed and transported more quickly. Such was the demand for the machines that they were often used by patients within an hour of production.

Visiting London in 1938 during another polio epidemic, Both produced additional respirators there which attracted the attention of William Morris (Lord Nuffield), a British motor manufacturer and philanthropist. Nuffield, intrigued by the design, financed the production of approximately 1700 machines at his car factory in Cowley, and donated them to hospitals throughout all parts of
Britain and the British Empire. Soon, the Both-Nuffield respirators were able to be produced by the thousand at about one-thirteenth the cost of the American design. By the early 1950s, there were over 700 Both-Nuffield iron lungs in the United Kingdom, but only 50 Drinker devices.

**Modern usage**

Rows of iron lungs filled hospital wards at the height of the polio outbreaks of the 1940s and 1950s, helping children and adults (mostly children) with bulbar polio and bulbospinal polio. A polio patient with paralyzed lungs could spend up to a week inside an iron lung.

Polio vaccination programs have virtually eradicated new cases of poliomyelitis in the United States. Because of this, and the development of modern ventilators, and widespread use of tracheal intubation and tracheotomy, the iron lung has mostly disappeared from modern medicine. In 1959, there were 1,200 people using tank respirators in the United States, but by 2004 there were only 39. By 2014, there were only 10 people left with an iron lung.

Positive pressure ventilation systems are now more common than negative pressure systems. Positive pressure ventilators work by blowing air into the patient’s lungs via intubation through the airway; they were used for the first time in Blegdams Hospital, Copenhagen, Denmark, during a polio outbreak in 1952. It proved a success and soon superseded the iron lung throughout Europe.

The iron lung now has a marginal place in modern respiratory therapy. Most patients with paralysis of the breathing muscles use modern mechanical ventilators that push air into the airway with positive pressure. These are generally efficacious and have the advantage of not restricting patients’ movements or caregivers’ ability to examine the patients as significantly as an iron lung does. However, negative pressure ventilation is a truer approximation of normal physiological breathing and results in more normal distribution of air in the lungs. It may also be preferable in certain rare conditions, such as central hypoventilation
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syndrome, in which failure of the medullary respiratory centers at the base of the brain results in patients having no autonomic control of breathing. At least one reported polio patient, Dianne Odell, had a spinal deformity that caused the use of mechanical ventilators to be contraindicated. There are patients who today still use the older machines, often in their homes, despite the occasional difficulty of finding the various replacement parts. Joan Headley of Post-Polio Health International said that as of May 28, 2008, there were about 30 patients in the U.S. still using an iron lung. That figure may be inaccurately low; Houston alone had 19 iron lung patients living at home in 2008. Martha Mason of Lattimore, North Carolina, died on May 4, 2009, after spending 60 of her 72 years in an iron lung.

On October 30, 2009, June Middleton of Melbourne, Australia, who had been entered in the Guinness Book of Records as the person who spent the longest time in an iron lung, died aged 83, having spent more than 60 years in her iron lung.

**Biphasic cuirass ventilation**

Biphasic cuirass ventilation (BCV) is a modern development of the iron lung, consisting of a wearable rigid upper-body shell (a cuirass) which functions as a negative pressure ventilator. The ventilation is biphasic because the cuirass is attached to a pump which actively controls both the inspiratory and expiratory phases of the respiratory cycle. This method is a modern improvement of ‘negative pressure ventilation’ (NPV), which could only control inspiratory breathing, relying on passive recoil for exhalation. BCV was developed by Dr Zamir Hayek, a pioneer in the field of assisted ventilation. Some of Dr Hayek’s previous inventions include the Hayek Oscillator, an early form of the technology.
Mechanical Ventilation in Neonates

Mechanical ventilation for neonates with respiratory failure, introduced in the 1960s and implemented widely in the 1970s, has resulted in a reduction in infant mortality. However, while this therapy has reduced the neonatal death rate from respiratory causes, the incidence of chronic lung disease, or bronchopulmonary dysplasia (BPD), continues to compromise long-term health.

Edwin Coombs, MA, RRT-NPS, ACCS, FAARC, director of marketing, Intensive Care & Neonatal Care North America, Dräger
Medical Inc, indicated that mechanical ventilation has become so advanced that few newborns nowadays die because of acute respiratory failure. “Mortality now is predominantly from other complications of extreme prematurity, such as infection, necrotizing enterocolitis and intracranial hemorrhage or congenital anomalies,” he said. “As a result, much focus has shifted from reducing mortality to reducing the incidence of chronic lung disease.”

OVERSIGHT, TREATMENT AND CHALLENGES

At Rainbow Babies and Children’s Hospital in Shaker Heights, Ohio, approximately 40 respiratory therapists attend high-risk deliveries as primary airway clinicians and also administer specialized care in the neonatal intensive care unit (NICU). The facility practices “tiering,” ie taking a step up or down as the patient’s condition improves or declines, according to John Gallagher, MPH, RRT-NPS.

He explained that when a neonate presents with surfactant deficiency, therapists begin non-invasive ventilation with facial CPAP using a Neotech RAM cannula to support respiratory function. “When they are intubated, we start a surfactant. When we deem [infants weighing less than 1500 grams] need ventilatory support, we start non-invasive ventilation following the basic respiratory distress syndrome criteria,” he added.

Gallagher pointed out that treating this population requires close monitoring. For instance, strict oxygen management is critical, with a goal of maintaining saturation between 90 and 95%. “Determining the appropriate vent setting for a 550 gram infant is challenging. You have to be precise. You can’t throw out a random number for a set of lungs that small,” he said.

Also, it’s essential to create optimal synchrony between the ventilator and the patient. “The vent wants to respond to what the patient is asking for. But a small patient has minute requests and their signals are less obvious,” Gallagher said, citing a narrow margin of error when treating neonates. “You’re dealing with lung
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tissue that is continuing to develop.” As the infant develops, settings need to be modified accordingly.

Carbon dioxide (CO₂) levels, among other indices, also require careful oversight. “Swings in CO₂ levels put the patient at risk for cerebral vascular damage,” Gallagher noted. “Modern ventilator platforms have a number of components that give real-time feedback on patient data.”

Rainbow Babies and Children’s Hospital uses transcutaneous CO₂ monitoring, endotracheal CO₂ monitoring and cerebral oximeters to obtain information the ventilator cannot provide. Therapists also monitor progress through a combination of chest radiography, arterial blood gas measurements and the baby’s own efforts. “We pull the pieces of information together,” Gallagher said.

To further reduce the chance of ventilator-associated injury, therapists at Rainbow Babies and Children’s Hospital follow aggressive weaning practices. Once patients are stable, they are liberated from mechanical ventilation and offered post-extubation support, noted Gallagher. “We are more willing to give kids a fighting chance, let them have the opportunity to breath on their own. If they fail, we replace the therapy,” he said. “Every day on the vent leads to more severe morbidity. We make every effort to wean early.”

Tidal Volume Accuracy/Loss a Concern

Tidal volume accuracy and understanding of compressible volume loss in the circuit rank as other important concerns when ventilating neonates. Today’s medical device market has a number of different ventilator models that address the issues of both volume control/pressure and endotracheal tube leaks.

For one, the Dräger Babylog VN500 utilizes a proximal airway sensor that measures both inspiratory delivery and expiratory return, which allows for the accurate measurement of tidal volume delivery as well as leakage percentage. Coombs said, “Babylog
VN500 takes this information into account and compensates automatically when ventilating neonates with set tidal volumes as low as 2 cm. Additionally, to support a clinician’s workflow and adapt to the infant’s changing ventilatory support requirements, the VN500 can provide invasive, non-invasive and oxygen therapy all within the one device.”

Pressure-limited, time-cycled, continuous flow ventilation has been the standard of care in neonatal ventilation for more than 30 years. But exceedingly high inspiratory pressures have been thought of as a chief contributing factor of lung injury, although the issue is not well understood. “One of the advantages cited for the preference for pressure-limited over volume-controlled ventilation has been the ability to directly control the inspiratory pressure. Over the past eight to ten years, a wealth of accumulated evidence shows that volume, rather than pressure, is the critical determinant of ventilator-induced lung injury,” Coombs said.

As a result of overwhelming evidence that excessive tidal volume, rather than high inspiratory pressure, is the primary determinant of lung injury, most clinicians now monitor the delivered tidal volume when using pressure-limited ventilation, volume-targeted ventilation or volume guarantee (VG).

The critical importance of distributing the tidal volume evenly into an optimally aerated lung has not been as widely appreciated and requires attention at the bedside. If extensive atelectasis is allowed to persist, the normal physiologic tidal volume entering the small proportion of open alveoli inevitably leads to over-expansion of the relatively healthy portion of the lung, with subsequent volutrauma and/or biotrauma, according to Coombs. The collapsed portion of the lung is also damaged, a condition known as atelectotrauma. So the benefits of volume-targeted ventilation cannot be realized without ensuring that the tidal volume is distributed evenly throughout the lungs.

“By design, the Dräger algorithm is geared toward slower adjustment for low tidal volume and more rapid adjustment for
low tidal volume and more rapid adjustment for excessive, potentially dangerous tidal volume,” he said.

In practical terms, optimization of lung inflation, referred to as the “open lung concept,” is achieved by applying adequate positive end-expiratory pressure (PEEP), Coombs continued. “It is important to understand that there is no single ‘safe’ PEEP level. Optimal end-expiratory pressure must be tailored to the degree of lung injury. For example, in infants who have no lung disease and, thus, normal lung compliance, a PEEP of 3 cm H₂O is probably appropriate, and a PEEP of 5 cm H₂O may result in overexpansion of the lungs, with impairment of venous return, elevated cerebral venous and systemic venous pressures, and decreased cardiac output,” he said. “Conversely, severely atelectatic, poorly compliant lungs may require PEEP levels as high as 8 to 10 cm H₂O or more to achieve adequate lung volume and improve the ventilation/perfusion ratio.”

In addition to monitoring tidal volume delivery to neonates, which should range between 2 and 5 mL, gas mixing needs to be supervised. “A teaspoon of gas gets delivered and ventilators need to know the delivery of that range of tidal volume. You have to monitor tidal volume as accurately as possible,” said Mark Rogers, RRT, RCP, senior product manager for CareFusion. “Some gas delivery systems deliver small tidal volume as well as accurate oxygen delivery. This is targeted to deliver consistent FIO2, but sometimes there are some fluctuations.”

VENTILATION CHALLENGES IN NEONATES

Rogers pointed out that babies’ lungs are stiff and non-compliant. CareFusion’s AVEA ventilator features volume guarantee in pressure control and in time cycled pressure limited for neonatal specific ventilation. With targeted ventilation, tidal volume might be lost to the patient circuit. “You need to monitor what gets into the lungs. If you have a flow sensor at the end of the trach tube, it helps to monitor this.” Proximal flow sensing
allows for accurate monitoring in the neonatal intensive care unit (NICU), which facilitates reliable triggering to help improve patient synchrony for these patients.

Ventilators with on-board compressors assist with transport, but still require an oxygen source, Rogers pointed out. The AVEA ventilator contains a scroll compressor and is able to operate for up to two hours on battery. For babies who are able to tolerate non-invasive ventilation, CareFusion provides NIV positive pressure ventilation via Infant Flow SiPAP System, a combination of nasal CPAP and Biphasic modalities.

Much like the tiered system at Rainbow Babies and Children’s Hospital, the “arc of acuity” follows the patient’s respiratory needs and responds accordingly, said Rogers. “You start the patient off with the least invasive technology. As the patient’s acuity increases, you meet the acuity and it goes down rapidly on the other side. The timeframe varies for switching from non-invasive ventilation to invasive ventilation,” he said. “Some hospitals may institute within minutes with invasive ventilation. In labor and delivery, they may start non-invasive ventilation. It depends on the underlying pathology.”

Whether clinicians use invasive or non-invasive ventilation, the procedures for newborns continue to pose some challenges. “In terms of ‘mechanical issues,’ there are inherent leaks due to the use of uncuffed endotracheal tubes during invasive ventilation,” said Coombs. “During noninvasive ventilation, the proper fit of a nasal or mask interface is paramount to minimize leaks and increase patient comfort. In either case, when leakage is excessive, this may lead to hypoventilation and hypercarbia.”

**Learning Curve**

Gallagher explained the facilities typically have only one or two ventilation platforms and with good reason. “Patient safety is number one. Limiting the number of platforms leads to a smoother learning curve for physicians, therapists, nurses and other staff. People have a better understanding and mastery of the
device," he said. "Also, you get a better deal if you buy in volume. If the facility purchases 25 machines, they get a better deal than they would if they bought two. Last, with different platforms you have reusable sensors, valves and disposable circuits. They are proprietary to each platform and need to be processed. Having control over the disposable and reusable parts is easier to do with a limited number of platforms. It reduces the chance of error and improves the workflow."

Depending on the device, the timeframe needed to learn and understand how to use the machine varies. For instance, the Babylog VN500 employs a user-intuitive interface that incorporates easy-to-read data, prioritizes alarm management, and provides for on-screen user support.

Coombs explained, "The interface can be configured to a variety of ways to accommodate clinician preferences, as well as provide for trended data screens up to seven days. Additionally, to support clinicians when using Dräger ventilation and neonatal products, our customers have access to the Intensive Care Online Network (ICON), which provides support 24/7/365 to discuss equipment, therapeutic management, and provide educational support."

CareFusion’s Rogers added that the learning curve might be a bit steeper for those who are moving from one platform to another. "For instance, you might be used to doing things one way and then have to change to do them another," he said, "but when you’re trained for a few days, it’s usually easy to operate the device. A post-sale education team at CareFusion trains respiratory therapists on the devices. It’s a patient safety issue." Rogers pointed out that CareFusion uses Simple Touch, which is a common user interface.

Hospital systems that purchased AVEA when it was first introduced in 2002 have the option of upgrading to the newest platform, which saves the facility money in the long run. "Those who bought the AVEA when it was initially released, don’t need to buy a new device. We make the new technology available to
existing customers," said Natasha Barany, product manager for AVEA ventilators. "The software system used with AVEA looks at greater practices surrounding the vent and increased measures and reporting. It saves time with paperwork and improves workflow." The Alaris pump, a smart integrated system, is the backbone and gives AVEA the ability to communicate better.

In today’s health care environment, it is critical that medical devices "talk to each other." Barany noted that CareFusion is currently devoting significant attention to communications as an area of development. She said that connectivity with the electronic medical record (EMR) allows for the transfer of important data through a portal, which serves as a repository of data.

"Software connects the device and makes the data meaningful for the hospital quality system," Barany said, noting that CareFusion currently transfers medical data for its adult patients this way. "The respiratory therapist looks at the data to see where the clinical process varies. This leads to better care and less time on the ventilator. You can measure and report data. The knowledge portal shows the respiratory therapist which patient may have a reportable health event. With neonates we’re looking at tracking the delivery of oxygen. This is very important in the care of neonates."

Coombs pointed out that the development of chronic lung disease in extremely preterm infants is multi-factorial, not always due to mechanical ventilation. "The degree of prematurity and presence of intrauterine inflammation have a very significant effect that may minimize the impact of a protective ventilation strategy," he said. "Thus, it will be difficult to demonstrate substantial differences in various ventilation strategies specific to long-term outcomes."

CONVENTIONAL MECHANICAL VENTILATION: TRADITIONAL AND NEW STRATEGIES

Important breakthroughs in neonatology, particularly in prevention and treatment of respiratory disorders, have extended
the limits of viability to lower gestational ages. Despite these advances, conventional mechanical ventilation (CMV) (usually pressure-limited intermittent mandatory ventilation in neonates) remains an essential therapy in neonatal intensive care. Advances in CMV, exogenous surfactant supplementation, and antenatal steroids have resulted in improved outcomes of critically ill neonates. Despite newer alternative ventilatory modes, such as high-frequency ventilation and patient-initiated mechanical ventilation, CMV continues to be the mainstay in the care of neonates.

Improved survival due to advances in neonatal care has resulted in an increased number of infants who are at risk for chronic lung disease and air leaks. Although the etiology of lung injury is multifactorial, recent animal and clinical data indicate that lung injury is largely dependent on the ventilatory strategies used. Optimal ventilatory strategies may improve the benefit-to-risk ratio by providing the best gas exchange with the smallest amount of lung injury. This chapter highlights the concepts of pulmonary mechanics, gas exchange, control of breathing, and lung injury that can be used to optimize CMV. Alternative modes of ventilation also are addressed. This evidenced-based review uses data from integrative studies (eg, meta-analyses, randomized clinical trials) whenever possible. However, because many controversies surrounding CMV have not been resolved with clinical studies, lesser levels of evidence are used as appropriate.

**Gas Exchange**

The general goal of CMV is to achieve normal blood gases, but ventilator adjustments also should be based on other factors, such as pulmonary mechanics, gas exchange mechanisms, control of breathing, and lung injury. A thorough understanding of these factors can help to guide the selection of ventilatory strategies. Neonates are vulnerable to impaired gas exchange, a common occurrence in this population, because of their high metabolic rate, decreased functional residual capacity, decreased compliance, and
potential for right-to-left shunts through the ductus arteriosus or foramen ovale. Hypercapnia and hypoxemia may coexist, although some disorders may affect gas exchange differentially.

**HYPERCAPNIA**

Hypercapnia usually is caused by hypoventilation or severe ventilation-perfusion mismatch. Carbon dioxide normally diffuses readily from the blood into the alveoli.

Elimination of carbon dioxide from the alveoli is directly proportional to alveolar minute ventilation, which is determined by the product of tidal volume (minus dead space ventilation) and frequency. Thus, the alveolar minute ventilation is calculated as:

![Figure: Relationships among various ventilator-controlled (shaded circles) and pulmonary mechanics (unshaded circles) that determine minute ventilation during pressure-limited, time-cycled ventilation.](image)

Figure: Relationships among various ventilator-controlled (shaded circles) and pulmonary mechanics (unshaded circles) that determine minute ventilation during pressure-limited, time-cycled ventilation.
The relationships between the circles joined by solid lines are described by simple mathematical equations. The dashed lines represent relationships that cannot be calculated precisely without considering other variables, such as pulmonary mechanics. Thus, simple mathematical equations determine the time constant of the lungs, the pressure gradient, and the inspiratory time. These, in turn, determine the delivered tidal volume, which when multiplied by the respiratory frequency, gives the minute ventilation. Alveolar ventilation can be calculated from the product of tidal volume and frequency when dead space is subtracted from the former.

\[
\text{alveolar minute ventilation} = (\text{tidal volume } - \text{ dead space}) \times \text{frequency}
\]

Tidal volume is the volume of gas inhaled (or exhaled) with each breath. Frequency is the number of breaths per minute. Dead space is that part of the tidal volume not involved in gas exchange, such as the volume of gas that fills the conducting airways. Because dead space is relatively constant, increases in either tidal volume or frequency increase alveolar ventilation and decrease PaCO\(_2\). Also, because dead space ventilation is constant, changes in tidal volume appear to be more effective at altering carbon dioxide elimination than alterations in frequency or other ventilatory parameters. For example, a 50% increase of tidal volume from 6 to 9 mL/kg, with dead space at a constant 3 mL/kg, doubles alveolar ventilation (from 3 to 6 mL/kg×frequency). However, increases in tidal volume may augment the risk of “volutrauma.” Tidal volume depends largely on the compliance of the respiratory system and on the pressure difference (ie, peak inspiratory pressure minus positive end expiratory pressure).

**HYPOXEMIA**

Hypoxemia is usually due to ventilation-perfusion mismatch or right-to-left shunting, although diffusion abnormalities and hypoventilation (eg, apnea) also may be at fault. Ventilation-perfusion mismatch is a major cause of hypoxemia in infants who have respiratory distress syndrome (RDS) and other types of
respiratory failure. Ventilation-perfusion mismatch usually is caused by poor ventilation of alveoli relative to their perfusion. Shunting can be intra- or extracardiac (eg, pulmonary).

During conventional ventilation, oxygenation is determined by the fraction of inspired oxygen concentration (FiO₂) and the mean airway pressure (MAP).

MAP is the average airway pressure during the respiratory cycle and can be calculated by dividing the area under the airway pressure curve by the duration of the cycle, from which the following equation is derived:

![Figure: Determinants of oxygenation during pressure-limited, time-cycled ventilation.](image)

Shaded circles represent ventilator-controlled variables. Solid lines represent the simple mathematical relationships that determine mean airway pressure and oxygenation, and dashed
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lines represent relationships that cannot be quantified with a simple mathematical method.

MAP = K (PIP - PEEP) (T_I/T_E) + PEEP

K is a constant determined by the flow rate and the rate of rise of the airway pressure curve, PIP is peak inspiratory pressure, PEEP is positive end-expiratory pressure, T_I is inspiratory time, and T_E is expiratory time. This equation indicates why MAP increases with increasing PIP, PEEP, inspiratory-to-expiratory time (I:E) ratio, and flow (increases K by creating a more square waveform).

The mechanism by which increases in MAP generally improve oxygenation seems to be the increased lung volume and improved ventilation-perfusion matching. Although there is a direct relationship between MAP and oxygenation, there are some exceptions. For the same change in MAP, increases in PIP and PEEP will enhance oxygenation more than will changes in the I:E ratio. Increases in PEEP are not as effective once an elevated level (>5 to 6 cm H_2O) is reached and may, in fact, not improve oxygenation at all for the following reasons.

A very high MAP may over-distend alveoli, leading to right-to-left shunting of blood in the lungs. If a very high MAP is transmitted to the intrathoracic structures, cardiac output may decrease, and thus, even with adequate oxygenation of blood, systemic oxygen transport (arterial oxygen content×cardiac output) may decrease. Blood oxygen content is largely dependent on oxygen saturation and hemoglobin level. It has been common to transfuse packed red blood cells into infants who have impaired oxygenation. Transfusion is most beneficial when anemia is severe (hematocrit <0.25 to 0.30 [<25% to 30%]). Oxygenation also depends on oxygen unloading at the tissue level, which is strongly determined by the oxygen dissociation curve. Acidosis and postnatal increases in 2,3-diphosphoglycerate and adult hemoglobin levels reduce oxygen affinity to hemoglobin, thereby favoring oxygen delivery to the tissues.
Pulmonary Mechanics

The interaction between the ventilator and the infant is strongly dependent on the mechanical properties of the respiratory system. A pressure gradient between the airway opening and the alveoli must exist to drive the flow of gases during both inspiration and expiration. The necessary pressure gradient is determined by the compliance, resistance, and inertance of the lungs and can be calculated from the equation of motion:

\[
\text{pressure} = \frac{\text{volume}}{\text{compliance}} + \text{resistance} \times \text{flow} + \text{inertance} \times \text{acceleration}
\]

Inertial forces during CMV are negligible when compared with compliance and resistance forces. Thus, the equation can be simplified to:

\[
\text{pressure} = \frac{\text{volume}}{\text{compliance}} + \text{resistance} \times \text{flow}
\]

Compliance

Compliance describes the elasticity or distensibility (e.g., lungs, chest wall, respiratory system) and is calculated from the change in volume per unit change in pressure:

\[
\text{compliance} = \frac{\Delta \text{volume}}{\Delta \text{pressure}}
\]

Therefore, the higher the compliance, the larger the delivered volume per unit of change in pressure. Normally, the chest wall is compliant in neonates and does not impose a substantial elastic load compared with the lungs. Total respiratory system compliance (lungs + chest wall) in neonates who have normal lungs ranges from 0.003 to 0.006 L/cm H₂O compared with compliance in neonates who have RDS, which may be as low as 0.0005 to 0.001 L/cm H₂O.

Resistance

Resistance describes the inherent capacity of the air conducting system (e.g., airways, endotracheal tube) and tissues to oppose airflow and is expressed as the change in pressure per unit change in flow:
resistance = \Delta \text{ pressure}/\Delta \text{ flow}

Airway resistance depends on: 1) radii of the airways (total cross-sectional area), 2) length of airways, 3) flow rate, and 4) density and viscosity of gas breathed. Distal airways normally contribute less to airway resistance because of their larger cross-sectional area, unless bronchospasm, mucosal edema, and interstitial edema decrease the lumen. Small endotracheal tubes that may contribute significantly to airway resistance are also important, especially when high flow rates that lead to turbulent flow are used. Total (airway + tissue) respiratory resistance values for normal neonates range from 20 to 40 cm H$_2$O/L/s and from 50 to 150 cm H$_2$O/L/s in intubated neonates.

**Time Constant**

Compliance and resistance can be used to describe the time necessary for an instantaneous or step change in airway pressure to equilibrate throughout the lungs. The time constant of the respiratory system is a measure of the time necessary for the alveolar pressure to reach 63% of the change in airway pressure. Time constant is the product of resistance and compliance, as follows:

\[ \text{Time constant} = \text{resistance} \times \text{compliance} \]

![Figure: Percentage change in pressure in relation to the time (in time constants) allowed for equilibration. As a longer time is allowed for equilibration, a higher percentage change in pressure will occur. The same rules govern the equilibration for step changes in volume.](image)
time constant = resistance × compliance

Thus, the time constant of the respiratory system is proportional to the compliance and the resistance. When a longer time is allowed for equilibration, a higher percentage of airway pressure will equilibrate throughout the lungs. For example, the lungs of a healthy neonate with a compliance of 0.004 L/cm H$_2$O and a resistance of 30 cm H$_2$O/L/s have a time constant of 0.12 seconds. The longer the duration of the inspiratory (or expiratory) time allowed for equilibration, the higher the percentage of equilibration. For practical purposes, delivery of pressure and volume is complete (95% to 99%) after three to five time constants.

Figure: Effects of incomplete inspiration (A) or incomplete expiration (B) on gas exchange.
The resulting time constant of 0.12 seconds indicates a need for an inspiratory or expiratory phase of 0.36 to 0.6 seconds. In contrast, lungs that have decreased compliance (such as in RDS) have a shorter time constant. Lungs that have a shorter time constant complete inflation and deflation faster than normal lungs. The clinical application of the concept of time constant is that very short inspiratory times may lead to incomplete delivery of tidal volume and, therefore, lower PIP and MAP, resulting in hypercapnia and hypoxemia.

An incomplete inspiration leads to decreases in tidal volume and mean airway pressure. Hypercapnia and hypoxemia may result. An incomplete expiration may lead to decreases in compliance and tidal volume and an increase in mean airway pressure. Hypercapnia with a decrease in PaO\textsubscript{2} may result. However, gas trapping and its resulting increase in mean airway pressure may decrease venous return, reducing cardiac output and impairing oxygen delivery.

Similarly, insufficient expiratory time may lead to increases in functional residual capacity and inadvertent PEEP, which are evidence of gas trapping that, in turn, decreases compliance and may impair cardiac output. A short expiratory time, a prolonged time constant, or an elevated tidal volume can result in gas trapping. Gas trapping during mechanical ventilation may manifest as carbon dioxide retention and lung hyperexpansion. Although PaO\textsubscript{2} may be adequate during gas trapping, venous return to the heart and cardiac output may be impaired, which can decrease oxygen delivery. Clinical findings that may suggest the presence of gas trapping include: 1) need for high ventilatory rates, 2) a prolonged time constant (eg, high resistance), 3) radiographic evidence of lung overexpansion, 4) decreased thoracic movement despite high PIP, and 5) impaired cardiovascular function (increased central venous pressure, decreased systemic blood pressure, metabolic acidosis, peripheral edema, and decreased urinary output).

Because values of compliance and resistance differ throughout inspiration and expiration, a single time constant cannot be
assumed. With heterogeneous lung disease, such as bronchopulmonary dysplasia, different lung regions may have different time constants because of varying compliances and resistances, partly accounting for the coexistence of atelectasis and hyperexpansion. The astute clinician can correlate changes in the time constant of the respiratory system to clinical events and interventions. Inspiratory or expiratory times then can be adjusted appropriately. In summary, the time necessary for lungs to inflate or deflate depends on the mechanical characteristics of this organ, specifically resistance and compliance.

In addition to using the clinical findings as well as compliance and resistance measurements to calculate time constant, a plot of volume-time or volume-flow can be used to make this estimation. The pattern of volume changes obtained by integrating the signal from a flow transducer can provide an estimate of the time constant. However, flow measurements are somewhat invasive, time-consuming, and frequently not available.

Furthermore, pulmonary mechanics are dynamic, frequently changing over time, and affected by adding a flow sensor to the gas delivery circuit.

An alternative technique that may be more useful in clinical practice is using chest wall motion as a semiquantitative estimate of tidal volume. Chest wall motion can be recorded with inductance plethysmography or other techniques.

At the bedside, chest wall motion can be measured with appropriately placed heart rate/respiration leads used for routine clinical monitoring. Careful visual assessment of chest wall motion can suffice. The shape of the inspiratory and expiratory phases can be analyzed. A rapid rise in inspiratory chest wall motion (or volume) with a plateau indicates complete inspiration. A rise without a plateau indicates incomplete inspiration. In this situation, prolongation of the inspiratory time results in more inspiratory chest wall motion and tidal volume delivery. A prolonged inspiratory plateau indicates that inspiratory time may be too
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long; shortening inspiratory time does not decrease inspiratory chest wall motion or tidal volume delivery and does not eliminate the plateau. The expiratory pattern of chest wall motion can be analyzed similarly.

Figure: Estimation of optimal inspiratory and expiratory times based on chest wall motion.

Control of Breathing

Important physiologic concepts of control of breathing need to be considered to understand some aspects of the interaction between the ventilator and the respiratory system. Respiratory drive is servocontrolled by the brain to minimize variations in arterial blood gases and pH despite changes in the efficiency of gas exchange and moment-to-moment changes in oxygen consumption and carbon dioxide production.

Ventilation is maintained by fine adjustments in tidal volume and respiratory rate that minimize the work of breathing. This fine adjustment is accomplished by motoneurons in the central nervous system that regulate inspiratory and expiratory muscles. These neurons receive input primarily from chemoreceptors and mechanoreceptors. These two components of respiratory control
provide feedback to adjust ventilation continuously. Mechanical ventilation results in changes in chemo-receptor and mechanoreceptor stimulation.

When \( \text{PaCO}_2 \) changes, ventilation is adjusted largely because of the activity of chemoreceptors in the brain stem. An increase in \( \text{PaCO}_2 \) increases respiratory drive. Because the chemoreceptors most likely sense the hydrogen ion concentration, metabolic acidosis and alkalosis have strong effects on respiratory drive that are somewhat independent of \( \text{PaCO}_2 \) values. In contrast, most of the changes in ventilation and respiratory drive produced by \( \text{PaO}_2 \) changes depend on the peripheral chemoreceptors, which include the carotid bodies and, to a lesser extent, the aortic bodies. In neonates, acute hypoxia produces a transient increase in ventilation that disappears quickly. Moderate or profound respiratory depression can be observed after a couple of minutes of hypoxia, and it is believed that this decline in respiratory drive is an important cause of hypoventilation or apnea in the newborn period.

It is also important to consider the role of mechanoreceptors in the regulation of breathing, particularly during neonatal life and infancy. Stretch receptors in airway smooth muscles respond to changes in tidal volume. For example, immediately following an inflation, a brief period of decreased or absent respiratory effort can be detected. This is called the Hering-Breuer inflation reflex, and usually it is observed in neonates during CMV when a large enough tidal volume is delivered. The presence of the Hering-Breuer inflation reflex is a clinical indication that a relatively good tidal volume is delivered. This reflex will be absent if the ventilator tidal volume is very small, such as when the endotracheal tube is plugged. The Hering-Breuer reflex is also time-related (ie, a longer inspiration tends to stimulate the reflex more). Thus, for the same tidal volume, a breath with a longer inspiratory time will elicit a stronger Hering-Breuer reflex and a longer respiratory pause.

At slow ventilator rates, large tidal volumes will stimulate augmented inspirations (Head paradoxical reflex). This reflex
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reflects improved lung compliance, and its occurrence is increased by administration of theophylline. This may be one of the mechanisms by which theophylline hastens weaning from CMV.

Mechanoreceptors also are altered by changes in functional residual capacity. An increase in functional residual capacity leads to a longer expiratory time because the next inspiratory effort is delayed. High continuous distending pressure (continuous positive airway pressure or PEEP) can prolong expiratory time and even decrease the respiratory rate due to the intercostal phrenic inhibitory and Hering-Breuer reflexes. Also, it is important to remember that during weaning from a ventilator, a high PEEP may decrease the spontaneous respiratory rate.

Other components of the mechanoreceptor system are the juxtamedullary (J) receptors, which are located in the interstitium of the alveolar wall and are stimulated by interstitial edema and fibrosis as well as by pulmonary capillary engorgement (e.g., congestive heart failure). Stimulation of the J receptors increases respiratory rate and may explain the rapid, shallow breathing frequently observed in patients who have these conditions.

Another reflex that affects breathing is the baroreflex. Arterial hypertension can lead to reflex hypoventilation or apnea through aortic and carotid sinus baroreceptors. Conversely, a decrease in blood pressure may result in hyperventilation.

VENTILATORY SUPPORT

Continuous Positive Airway Pressure (CPAP)

CPAP has been an important tool in the treatment of neonates who have RDS. The mechanisms by which CPAP produces its beneficial effects include: 1) increased alveolar volumes, 2) alveolar recruitment and stability, and 3) redistribution of lung water. The results are usually an improvement in ventilation-perfusion matching. However, high CPAP levels may lead to side effects.

Multiple clinical trials have evaluated the use of CPAP in neonates who have respiratory disorders. Meta-analyses generally
conclude that CPAP is most beneficial early in the therapy of neonates who have established RDS. Prophylactic CPAP in preterm infants does not decrease the incidence or severity of RDS and does not reduce the rate of complications or death. Once the diagnosis of RDS is established, the administration of CPAP decreases oxygen requirements and the need for mechanical ventilation and may reduce mortality. However, the incidence of air leaks is increased among infants who receive CPAP. The optimal time to start CPAP depends on the severity of RDS. “Early” CPAP (ie, when the arterial-to-alveolar oxygen ratio is approximately higher than 0.20) decreases the subsequent need for CMV and the duration of respiratory assistance. These meta-analyses suggest that CPAP should be initiated in newborns who have RDS, for example, when the PaO$_2$ is approximately less than 50 torr and the FiO$_2$ is 0.40 or more. Studies performed to determine whether CPAP facilitates successful extubation have not shown consistent results.

CMV

Strategies for optimizing CMV have been developed based on principles of pulmonary mechanics and gas exchange. It has been shown that these ventilatory strategies result in more frequent improvement of blood gases than ventilatory changes that follow alternate decisions. Nonetheless, the complexities of the multiple patient presentations and available ventilatory changes result in continued controversy in this area. Much research remains to be done to clarify the relationship between the optimal ventilatory pattern and the underlying lung pathology.

PIP

Changes in PIP affect both PaO$_2$ (by altering the MAP) and PaCO$_2$ (by its effects on tidal volume and, thus, alveolar ventilation). Therefore, an increase in PIP will improve oxygenation and decrease PaCO$_2$. A high PIP should be used cautiously because it may increase the risk of volutrauma, with resultant air leaks and bronchopulmonary dysplasia. Tidal volume can be measured, but
in most clinical settings, breath sounds, chest excursions, and respiratory reflexes are good indicators of appropriate tidal volume.

A common mistake made by clinicians is to relate PIP to weight (e.g., the misconception that larger infants need a higher PIP). Rather, PIP requirements are strongly determined by the compliance of the respiratory system, and larger infants tend to have more compliant lungs, therefore requiring a lower PIP. In addition to compliance, the factors that should be considered in selecting the PIP level are blood gas derangements, chest rise, and breath sounds. In contrast, weight, resistance, time constant, and PEEP should not be considered in the selection of the level of PIP.

**PEEP**

Adequate PEEP prevents alveolar collapse, maintains lung volume at end expiration, and improves ventilation-perfusion matching. Increases in PEEP will raise MAP and functional residual capacity, thereby improving oxygenation. Nonetheless, use of a very elevated PEEP does not benefit oxygenation consistently. For example, older infants who have chronic lung disease may tolerate higher levels of PEEP with improvement in oxygenation, but a very high PEEP may decrease venous return, cardiac output, and oxygen transport and increase pulmonary vascular resistance. It is important to emphasize that although increases in both PIP and PEEP will increase MAP and oxygenation, they usually have opposite effects on carbon dioxide elimination. By altering the delta pressure (PIP minus PEEP), an elevation of PEEP may decrease tidal volume and carbon dioxide elimination and, therefore, increase PaCO\(_2\). However, if functional residual capacity is low, an increase in PEEP may improve ventilation-perfusion matching and relieve both hypoxemia and hypercapnia.

Various approaches have been proposed to optimize the effects of PEEP. These include efforts to reduce the physiologic shunt fraction, improve lung compliance, increase maximal oxygen delivery, and improve cardiac output. PEEP in the range of 4 to 6 cm H\(_2\)O improves oxygenation in neonates who have RDS without
compromising lung mechanics, carbon dioxide elimination, or hemodynamic stability. Careful assessment of tidal volumes and carbon dioxide elimination suggests that PEEP levels in the lower end of this range may be preferable in infants who have RDS. PEEP has a variable effect on lung compliance. An initial improvement in compliance occurs in response to low levels of end expiratory pressure, but it may worsen at higher levels of PEEP (>5 to 6 cm H$_2$O).

**RATE**

Changes in frequency alter alveolar minute ventilation and, thus, PaCO$_2$. In large randomized trials, relatively high ventilatory rates (60 breaths/min) resulted in a decreased incidence of pneumothorax in preterm infants who had RDS. An individualized approach should be taken, with the goal of providing adequate minute ventilation using minimal mechanical force.

Generally, a high rate, low tidal volume strategy is preferred. However, if a very short expiratory time is employed, expiration may be incomplete.

The gas trapped in the lungs can increase functional residual capacity and place the infant on the flat part of the pressure-volume curve, thus decreasing lung compliance. Furthermore, tidal volume decreases as inspiratory time is reduced beyond a critical level, depending on the time constant of the respiratory system. Thus, minute ventilation is not a linear function of frequency above a certain ventilator rate during pressure-limited ventilation. Alveolar ventilation actually may fall with higher ventilatory rates as tidal volumes approach the volume of the anatomic dead space when inspiratory or expiratory times become insufficient.

Frequency changes alone (with a constant I:E ratio) usually do not alter MAP or substantially affect PaO$_2$. In contrast, any changes in T$_1$ that accompany frequency adjustments may affect the airway pressure waveform and, thus, alter MAP and oxygenation.
**I:E RATIO**

The major effect of an increase in the I:E ratio is to increase MAP and improve oxygenation. However, when corrected for MAP, changes in the I:E ratio are not as effective in increasing oxygenation as are changes in PIP or PEEP. A reversed I:E ratio (inspiratory time longer than expiratory time) as high as 4:1 has been shown to be effective in increasing PaO₂, but side effects may occur. Although one study suggested a decreased incidence of bronchopulmonary dysplasia with the use of reversed I:E ratios, a large, well-controlled, randomized trial has revealed only reductions in the duration of a high inspired oxygen concentration and PEEP exposure with reversed I:E ratios and no differences in morbidity or mortality. Changes in the I:E ratio usually do not alter tidal volume unless T_I and T_E become relatively too short. Thus, carbon dioxide elimination usually is not altered by changes in I:E ratio.

**T_I AND T_E**

The effects of changes in T_I and T_E on gas exchange are strongly influenced by the relationships of these times to the inspiratory and expiratory time constant, respectively. A T_I that is three to five times longer than the time constant of the respiratory system allows relatively complete inspiration. A long T_I increases the risk of pneumothorax. Shortening T_I is advantageous during weaning. In a randomized trial, limitation of T_I to 0.5 seconds rather than 1.0 second resulted in a significantly shorter duration of weaning. In contrast, patients who have chronic lung disease may have a prolonged time constant. In these patients, a longer T_I (around 0.8 sec) may result in improved tidal volume and better carbon dioxide elimination.

**FiO₂**

Changes in FiO₂ alter alveolar oxygen pressure and, thus, oxygenation. Because FiO₂ and MAP both determine oxygenation, they can be balanced as follows. During increasing support, FiO₂
is increased initially until it reaches about 0.6 to 0.7, when additional increases in MAP are warranted. During weaning, \( \text{FiO}_2 \) is decreased initially (to about 0.4 to 0.7) before MAP is reduced because maintaining an appropriate MAP may allow substantial reduction in \( \text{FiO}_2 \). MAP should be reduced before a very low \( \text{FiO}_2 \) is reached because a higher incidence of air leaks has been observed if distending pressures are not weaned earlier.

**FLOW**

Changes in flow have not been well studied in infants, but they probably affect arterial blood gases minimally as long as a sufficient flow is used. In general, flows of 8 to 12 L/min are sufficient in most neonates. High flows are needed when inspiratory time is shortened to maintain an adequate tidal volume.

**PATHOPHYSIOLOGY-BASED VENTILATORY STRATEGIES**

RDS is characterized by low compliance and low functional residual capacity. An optimal CMV strategy may include conservative indications for CMV, the lowest PIP and tidal volume required, moderate PEEP (3 to 5 cm H\(_2\)O), permissive hypercapnia, judicious use of sedation/paralysis, and aggressive weaning.

Chronic lung disease is usually heterogeneous, with varying time constants among lung areas. Resistance may be markedly increased, and frequent exacerbations may occur. A higher PEEP (4 to 6 cm H\(_2\)O) often is used, and longer T\(_I\)s and T\(_E\)s with low flow rates are preferred. Hypercarbia and a compensated respiratory acidosis often are tolerated to avoid increasing lung injury with aggressive CMV.

Persistent pulmonary hypertension of the neonate may be primary or associated with meconium aspiration syndrome, prolonged intrauterine hypoxia, congenital diaphragmatic hernia, or other causes. Ventilatory management of these infants often is controversial and varies markedly among centers. In general, \( \text{FiO}_2 \) is adjusted to maintain Pao\(_2\) between 80 and 100 torr to minimize...
Mechanical Ventilation in Neonates

hypoxia-mediated pulmonary vasoconstriction. Ventilatory rates and pressures are adjusted to maintain an arterial pH between 7.45 and 7.55. Care should be taken to prevent extremely low Paco₂ (<20 torr), which can cause cerebral vasoconstriction. The addition of inhaled nitric oxide to CMV reduces the need for extracorporeal membrane oxygenation.

STRATEGIES TO PREVENT LUNG INJURY

Recently emphasis is being placed on the evidence that lung injury is partially dependent on the particular ventilatory strategies used. There is an emerging consensus that CMV leads to lung injury. It has been recommended that clinicians use more gentle ventilatory strategies in which gas trapping and alveolar overdistention are minimized while blood gas targets are modified to accept higher-than-normal Paco₂ values and lower-than-normal Pao₂ values. There has been interest in a variety of strategies of CMV that may reduce the risk of lung injury in neonates.

Ventilator-associated lung injury traditionally has been thought to be due to the use of high pressures; thus, the term barotrauma. However, recent laboratory-based and clinical research has raised questions about this purported mechanism.

Experimentally, investigators have used high and low volumes and pressures in an attempt to determine if volume or pressure is the major culprit responsible for lung injury in the immature animal. Using negative pressure ventilation and chest strapping, investigators have dissociated the magnitudes of volumes and pressures.

These studies consistently demonstrate that markers of lung injury (pulmonary edema, epithelial injury, and hyaline membranes) are present with the use of high volume and low pressure, but not with the use of low volume and high pressure. Thus, many investigators and clinicians prefer the term volutrauma to the more classic term of barotrauma. The heterogeneity of lung tissue involvement in many respiratory diseases predisposes some
parts of the lung to volutrauma. Oxidant injury may be another serious cause of ventilator-associated lung injury. Furthermore, immature lungs are particularly susceptible to lung injury.

**Permissive Hypercapnia**

Permissive hypercapnia, or controlled mechanical hypoventilation, is a strategy for the management of patients receiving ventilatory assistance. When using this strategy, priority is given to the prevention or limitation of overventilation rather than to maintenance of normal blood gases and the high alveolar ventilation that frequently is used. It is beginning to be recognized that respiratory acidosis and alveolar hypoventilation may be an acceptable price for the prevention of pulmonary volutrauma. Two large retrospective studies designed to determine risk factors for lung injury in neonates concurred on the potential importance of this ventilatory strategy, noting that higher Paco$_2$ values were associated with less lung injury. Using multiple logistic regression, these two studies independently concluded that ventilatory strategies leading to hypocapnia during the early neonatal course resulted in an increased risk of lung injury. Thus, it is possible that ventilatory strategies that tolerate mild hypercapnia or prevent hypocapnia, particularly during the first days of life, result in a reduced incidence and severity of lung injury.

We performed a study to determine whether a ventilatory strategy of permissive hypercapnia reduces the duration of assisted ventilation in surfactant-treated neonates. Surfactant-treated infants (birthweight 854 ±163 g; gestational age 26 ± 1.4 wk) receiving assisted ventilation during the first 24 hours after birth were randomized to permissive hypercapnia (Paco$_2$ 45 to 55 mm Hg) or to normocapnia (Paco$_2$ 35 to 45 mm Hg). The number of patients receiving assisted ventilation during the intervention period was lower in the permissive hypercapnia group ($P <$0.005). During that period, the ventilated patients in the permissive hypercapnia group had a higher Paco$_2$ and lower PIP, MAP, and ventilator rate than those in the normocapnia group. Larger studies to determine if
permissive hypercapnia improves major outcome measures are warranted.

**Low Tidal Volume Ventilation**

Ventilatory strategies for CMV in infants should focus on prevention of overdistention, use of relatively small tidal volumes, maintenance of adequate functional residual capacity, and use of sufficient $T_i$ and $T_e$. Because high maximal lung volume appears to correlate best with lung injury, selection of an appropriate PIP and the functional residual capacity (or operating lung volume) are critical to preventing lung injury during pressure-limited ventilation. With the recognition that large tidal volumes lead to lung injury, relatively small tidal volumes now are recommended. Studies in healthy infants report tidal volumes to range from 5 to 8 mL/kg compared with 4 to 6 mL/kg among infants who have RDS. In our pilot study, tidal volumes of 4 to 5 mL/kg per minute generally were used in infants in the permissive hypercapnia group (unpublished observations). However, insufficient data are available to recommend a specific size of tidal volume in these infants. It should be noted that infants who have severe pulmonary disease should be ventilated with small tidal volumes because lung heterogeneity and unexpanded alveoli will lead to overdistention and injury of the most compliant alveoli if a “normal” tidal volume is used. Nonetheless, maintenance of an adequate functional residual capacity is also necessary.

**STRATEGIES BASED ON ALTERNATIVE MODES OF VENTILATION**

Technological advances, including improvement in flow delivery systems, breath termination criteria, guaranteed tidal volume delivery, stability of PEEP, air leak compensation, prevention of pressure overshoot, on-line pulmonary function monitoring, and triggering systems, have resulted in better ventilators. Patient-initiated mechanical ventilation, patient-triggered ventilation, and synchronized intermittent mandatory
ventilation are being used increasingly in neonates. High-frequency ventilation is another mode that may reduce lung injury and improve pulmonary outcome.

**Patient-triggered Ventilation**

The most frequently used ventilators in neonates are time-triggered at a preset frequency, but because of the available bias flow, the patient also can take spontaneous breaths.

In contrast, patient-triggered ventilation (also called assist/control) uses spontaneous respiratory efforts to trigger the ventilator. With pressure-triggered ventilation airflow, chest wall movement, airway pressure, or esophageal pressure is used as an indicator of the onset of the inspiratory effort.

Once the ventilator detects an inspiratory effort, it delivers a ventilator breath of predetermined settings (PIP, inspiratory duration, and flow). Although improved oxygenation has been observed, patient-triggered ventilation frequently needs to be discontinued in some very immature infants because of weak respiratory efforts. A backup rate may be used to reduce this problem.

**Synchronized Intermittent Mandatory Ventilation**

This mode of ventilation achieves synchrony between the patient and the ventilator breaths. Synchrony easily occurs in most neonates because strong respiratory reflexes during early life elicit relaxation of respiratory muscles at the end of lung inflation. Furthermore, inspiratory efforts usually start when lung volume is decreased at the end of exhalation. Synchrony may be achieved by nearly matching the ventilator frequency to the spontaneous respiratory rate or by simply ventilating at relatively high rates (60 to 120 breaths/min). Triggering systems can be used to achieve synchronization when synchrony does not occur with these maneuvers. Synchronized intermittent mandatory ventilation is as effective as CMV, but no major benefits were observed in a large randomized controlled trial.
**Proportional Assist Ventilation**

Both patient-triggered ventilation and synchronized intermittent mandatory ventilation are designed to synchronize only the onset of the inspiratory support. In contrast, proportional assist ventilation matches the onset and duration of both inspiratory and expiratory support. Furthermore, ventilatory support is in proportion to the volume and flow of the spontaneous breath. Thus, the ventilator can decrease the elastic or resistive work of breathing selectively. The magnitude of the support can be adjusted according to the patient’s needs. When compared with conventional and patient-triggered ventilation, proportional assist ventilation reduces ventilatory pressures while maintaining or improving gas exchange. Randomized clinical trials are needed to determine if proportional assist ventilation leads to major benefits compared with CMV.

**Tracheal Gas Insufflation**

The added dead space of the endotracheal tube and the ventilator adapter that connects to the endotracheal tube contributes to the anatomic dead space and reduces alveolar minute ventilation, leading to reduced carbon dioxide elimination. In smaller infants or with increasing severity of pulmonary disease, dead space becomes the largest proportion of the tidal volume. With tracheal gas insufflation, gas delivered to the distal part of the endotracheal tube during exhalation washes out this dead space and the accompanying carbon dioxide. Tracheal gas insufflation results in a decrease in PaCO₂, PIP, or both. If proven safe and effective, tracheal gas insufflation should be useful in reducing tidal volume and the accompanying volutrauma, particularly in very preterm infants and infants who have very decreased lung compliance.

**High-frequency Ventilation**

Because of its potential to reduce volutrauma, there has been a surge of interest in high-frequency ventilation in the past few years. High-frequency ventilation may improve blood gases
because, in addition to the gas transport by convection, other mechanisms of gas exchange may become active at high frequencies. There has been extensive clinical use of various high-frequency ventilators in neonates. Controlled trials with high-frequency positive pressure using rates of 60 breaths/min (versus 30 to 40 breaths/min for CMV) reported a decreased incidence of air leaks. Small randomized trials suggest that bronchopulmonary dysplasia may be prevented with high-frequency jet ventilation, but results are inconclusive. The largest randomized trial of high-frequency ventilation revealed that early use of high-frequency oscillatory ventilation did not improve outcome. Although various randomized controlled trials show heterogeneous results, meta-analyses largely confirm the original findings. However, there are trends toward decreases in bronchopulmonary dysplasia/chronic lung disease, but increases in severe intraventricular hemorrhage and periventricular leukomalacia as well as small increases in air leaks with high-frequency oscillatory ventilation or high-frequency flow interrupters. High-frequency ventilation is a safe alternative for infants who fail CMV.
Development of the Respiratory System

The respiratory system does not carry out its physiological function (of gas exchange) until after birth. The respiratory tract, diaphragm and lungs do form early in embryonic development. The respiratory tract is divided anatomically into 2 main parts:

1. upper respiratory tract, consisting of the nose, nasal cavity and the pharynx
2. lower respiratory tract consisting of the larynx, trachea, bronchi and the lungs.

In the head/neck region, the pharynx forms a major arched cavity within the pharyngeal arches. The lungs go through 4 distinct histological phases of development and in late fetal development thyroid hormone, respiratory motions and amniotic fluid are thought to have a role in lung maturation. The two main respiratory cell types, squamous alveolar type 1 and alveolar type 2 (surfactant secreting), both arise from the same bi-potential progenitor cell. The third main cell type are macrophages (dust cells) that arise from blood monocyte cells.

Development of this system is not completed until the last weeks of Fetal development, just before birth. Therefore premature babies have difficulties associated with insufficient surfactant (end month 6 alveolar cells type 2 appear and begin to secrete surfactant).
 Week 4 - laryngotracheal groove forms on floor foregut.
 Week 5 - left and right lung buds push into the pericardioperitoneal canals (primordia of pleural cavity)
 Week 6 - descent of heart and lungs into thorax. Pleuroperitoneal foramen closes.
 Week 7 - enlargement of liver stops descent of heart and lungs.
 Month 3-6 - lungs appear glandular, end month 6 alveolar cells type 2 appear and begin to secrete surfactant.
 Month 7 - respiratory bronchioles proliferate and end in alveolar ducts and sacs.

LUNG DEVELOPMENT STAGES

Human Lung Stages

<table>
<thead>
<tr>
<th>Stage</th>
<th>Human</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embryonic</td>
<td>week 4 to 5</td>
<td>lung buds originate as an outgrowth from the ventral wall of the foregut where lobar division occurs</td>
</tr>
<tr>
<td>Pseudoglandular</td>
<td>week 5 to 17</td>
<td>conducting epithelial tubes surrounded by thick mesenchyme are formed, extensive airway branching</td>
</tr>
<tr>
<td>Canalicular</td>
<td>week 16 to 25</td>
<td>bronchioles are produced, increasing number of capillaries in close contact with cuboidal</td>
</tr>
</tbody>
</table>
epithelium and the beginning of alveolar epithelium development

Saccular  week 24 to 40  alveolar ducts and air sacs are developed

Alveolar  late fetal to 8 years  secondary septation occurs, marked increase of the number and size of capillaries and alveoli

The sequence is most important rather than the actual timing, which is variable in the existing literature.
Canalicular stage
  • week 16 - 24
  • Lung morphology changes dramatically
  • differentiation of the pulmonary epithelium results in the formation of the future air-blood tissue barrier.
  • Surfactant synthesis and the canalization of the lung parenchyma by capillaries begin.
  • future gas exchange regions can be distinguished from the future conducting airways of the lungs.

Pseudoglandular stage

*Respiratory histology (week 8)*

  • week 5 - 17
  • tubular branching of the human lung airways continues
  • by 2 months all segmental bronchi are present.
  • lungs have appearance of a glandlike structure.
  • stage is critical for the formation of all conducting airways.
  • lined with tall columnar epithelium, the more distal structures are lined with cuboidal epithelium.
Development of the Respiratory System

Human lung pseudoglandular stage

Saccular stage

- week 24 to near term.
- most peripheral airways form widened airspaces, termed saccules.
- saccules widen and lengthen the airspace (by the addition of new generations).
future gas exchange region expands significantly.

Fibroblastic cells also undergo differentiation, they produce extracellular matrix, collagen, and elastin. May have a role in epithelial differentiation and control of surfactant secretion.

The vascular tree also grows in length and diameter during this time.

Alveolar stage

- near term through postnatal period.
- 1-3 years postnatally alveoli continue to form through a septation process increasing the gas exchange surface area.
- microvascular maturation occurs during this period.
- respiratory motions and amniotic fluid are thought to have a role in lung maturation.

Premature babies have difficulties associated with insufficient surfactant (end month 6 alveolar cells type 2 appear and begin to secrete surfactant).
Development of the Respiratory System

Respiratory secondary septum

Respiratory species comparison

Mouse lung development
Pediatric and Neonatal Mechanical Ventilation

<table>
<thead>
<tr>
<th>Species</th>
<th>Term</th>
<th>Embryonic</th>
<th>Pseudoglandular</th>
<th>Canalicular</th>
<th>Sacellular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human</td>
<td>280</td>
<td>&lt; 42</td>
<td>52 - 112</td>
<td>112 - 168</td>
<td>168</td>
</tr>
<tr>
<td>Primate</td>
<td>168</td>
<td>&lt; 42</td>
<td>57 - 80</td>
<td>80 - 140</td>
<td>140</td>
</tr>
<tr>
<td>Sheep</td>
<td>150</td>
<td>&lt; 40</td>
<td>40 - 80</td>
<td>80 - 120</td>
<td>120</td>
</tr>
<tr>
<td>Rabbit</td>
<td>32</td>
<td>&lt; 18</td>
<td>21 - 24</td>
<td>24 - 27</td>
<td>27</td>
</tr>
<tr>
<td>Rat</td>
<td>22</td>
<td>&lt; 13</td>
<td>16 - 19</td>
<td>19 - 20</td>
<td>21</td>
</tr>
<tr>
<td>Mouse</td>
<td>20</td>
<td>&lt; 9</td>
<td>16</td>
<td>18</td>
<td>19</td>
</tr>
</tbody>
</table>

**Mouse**

The following images are from a recent study of the development of bronchial branching in the mouse between E10 to E14.

Mesenchyme (red) and epithelium (blue) the study used knockout mice to show the role of Wnt signalling in branching morphogenesis.

*Mouse Development*
Embryonic Respiratory Development

Pseudoglandular Respiratory Development

*Pseudoglandular period identified in this chapter (GA weeks 12 to 16)*

Human lung at pseudoglandular stage showing E- and N-cadherin and α-catenin localization.
ENDOCRINE LUNG

Neonatal Human

Pulmonary neuroendocrine cell (EM)

Fetal Rabbit

Neuroepithelial body
Development of the Respiratory System

Pulmonary neuroendocrine cells (PNECs)

- develop in late embryonic to early fetal period.
- later in mid-fetal period clusters of these cells form neuroepithelial bodies (NEBs).
- first cell type to differentiate in the airway epithelium.
  - differentiation regulated by proneural genes - mammalian homolog of the achaete-scute complex (Mash-1) and hairy and enhancer of split1 (Hes-1).
- located in the fetal lung at bronchiole branching points.
- may stimulate mitosis to increase branching.
- secrete 2 peptides - gastrin-releasing peptide (GRP) and calcitonin gene related peptide (CGRP)

Lung Histology

Birth Changes

At birth the lung epithelium changes from a prenatal secretory to a postnatal absorptive function. Several factors have been
identified as influencing this transport change including: epinephrine, oxygen, glucocorticoids, and thyroid hormones.

**Lung Cardiovascular**

Pulmonary Circulation

- pulmonary arteries and veins arise by vasculogenesis

Pulmonary Veins

- vasculogenesis in the mesenchyme surrounding the terminal buds during the pseudoglandular stage.
  - vasculogenesis - describes the formation of new blood vessels from pluripotent precursor cells.
- angiogenesis in the canalicular and alveolar stages.
  - angiogenesis - describes the formation of new vessels from pre-existing vessels.

**Bronchial Circulation**

Bronchial Arteries

- vascularising the walls of the airways and the large pulmonary vessels providing giving oxygen and nutrients.
- extend within the bronchial tree to the periphery of the alveolar ducts.
- not found in the lungs until around 8 weeks of gestation.
  - one or two small vessels extend from the dorsal aorta and run into the lung alongside the cartilage plates of the main bronchus.

Bronchial Veins

- small bronchial veins within the airway wall drain into the pulmonary veins.
- large bronchial veins seen close to the hilum and drain into the cardinal veins and the right atrium.

**MOLECULAR**

- Nkx2-1 (Titf1) - ventral wall of the anterior foregut, identifies the future trachea.
Development of the Respiratory System

- Localized Fgf10 expression not required for lung branching but prevents epithelial differentiation “As the lung buds grow out, proximal epithelial cells become further and further displaced from the distal source of Fgf10 and differentiate into bronchial epithelial cells. Interestingly, our data presented here show that once epithelial cells are committed to the Sox2-positive airway epithelial cell fate, Fgf10 prevents ciliated cell differentiation and promotes basal cell differentiation.”

- Opposing Fgf and Bmp activities regulate the specification of olfactory sensory and respiratory epithelial cell fates “In this study, we provide evidence that in both chick and mouse, Bmp signals promote respiratory epithelial character, whereas Fgf signals are required for the generation of sensory epithelial cells. Moreover, olfactory placodal cells can switch between sensory and respiratory epithelial cell fates in response to Fgf and Bmp activity, respectively. Our results provide evidence that Fgf activity suppresses and restricts the ability of Bmp signals to induce respiratory cell fate in the nasal epithelium.”

- Heparan sulfate in lung morphogenesis “Heparan sulfate (HS) is a structurally complex polysaccharide located on the cell surface and in the extracellular matrix, where it participates in numerous biological processes through interactions with a vast number of regulatory proteins such as growth factors and morphogens....the potential contribution of HS to abnormalities of lung development has yet to be explored to any significant extent, which is somewhat surprising given the abnormal lung phenotype exhibited by mutant mice synthesizing abnormal HS.”

- Signaling via Alk5 controls the ontogeny of lung Clara cells “Clara cells, together with ciliated and pulmonary neuroendocrine cells, make up the epithelium of the bronchioles along the conducting airways. Clara cells are also known as progenitor or stem cells during lung
Pediatric and Neonatal Mechanical Ventilation

regeneration after injury....Using lung epithelial cells, we show that Alk5-regulated Hes1 expression is stimulated through Pten and the MEK/ERK and PI3K/AKT pathways. Thus, the signaling pathway by which TGFbeta/ALK5 regulates Clara cell differentiation may entail inhibition of Pten expression, which in turn activates ERK and AKT phosphorylation.”

• Wt1 and retinoic acid signaling in the subcoelomic mesenchyme control the development of the pleuropericardial membranes and the sinus horns “Pericardium and sinus horn formation are coupled and depend on the expansion and correct temporal release of pleuropericardial membranes from the underlying subcoelomic mesenchyme. Wt1 and downstream Raldh2/retinoic acid signaling are crucial regulators of this process.”

DEVELOPMENT OF THE RESPIRATORY SYSTEM

Formation of the lung buds

When the embryo is approximately 4 weeks old, the respiratory diverticulum (lung bud) appears as an outgrowth from the ventral wall of the foregut. An increase in retinoic acid causes upregulation of the transcription factor TBX4 that will induce formation of the bud, growth and differentiation of the lungs. The epithelium of the internal lining of the larynx, trachea, bronchi and lungs is entirely of endodermal origin. The cartilagenous, muscular and connective tissue of trachea and lungs are derived from splanchnic mesoderm.

1. The lung bud is in open communication with the foregut.
2. The diverticulum expands caudally and two tracheoesophageal ridges separate it from the foregut.
3. Tracheoesophageal ridges fuse - tracheoesophageal septum.
4. The foregut is divided into a:
   - dorsal portion – esophagus
   - ventral portion – trachea and lung buds
The internal lining of the larynx originates from endoderm, but the cartilages and muscles originate from mesenchyme of the fourth and sixth pharyngeal arches. As a result of rapid proliferation of this mesenchyme, the laryngeal orifice changes in appearance from a sagittal slit to a T-shaped opening.

When the mesenchyme of the two arches transforms into the thyroid, cricoid and arytenoid cartilages the adult shape of the laryngeal orifice can be recognized. The laryngeal epithelium proliferates rapidly, resulting in a temporary occlusion of the lumen.

Subsequently, vacuolization and recanalization produces a pair of lateral recesses, the laryngeal ventricles that are bounded by folds of tissue that differentiate into the false and true vocal cords. Since musculature of the larynx is derived from mesenchyme of the fourth and sixth pharyngeal arches, all laryngeal muscles are innervated by branches of vagus nerve (the superior laryngeal
nerve innervates derivatives of the fourth paryngeal arch and the recurrente nerve innervates derivatives of the sixth laryngeal arch).

**Trachea, bronchi and lungs**

During its separation from the foregut, the lung bud forms the trachea and two bronchial buds. At the beginig of the fifth week, each of these buds enlarges and form right and left main bronchi. The right main bronchi gives rise to three secondary bronchi and the left main bronchi forms two secondary bronchi. During further development, secondary bronchi divide repeatedly, forming ten tertiary (segmental) bronchi in the right lung and eight in the left, creating the bronchopulmonary segments of the adult lung.

With subsequent growth, the lung expands into the pericardioperitoneal canals. Pleuroperitoneal and pleuropericardial folds separate the pericardioperitoneal canals from the peritoneal and pericardial cavities, respectively.

The lung bud forms the trachea and two lateral outpockets - bronchial buds that will form the right and left main bronchi. In the lungs the mesoderm which covers the outside of the lung will give rise to visceral pleura; the somatic mesoderm layer which
covers the body wall from the inside will become the parietal pleura. The pleural cavity is the space between the parietal and visceral pleura.

Maturation of the lungs

<table>
<thead>
<tr>
<th>Periods</th>
<th>time</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudoglandular</td>
<td>5 – 16 week</td>
<td>Branching has continued to form terminal bronchioles. No respiratory bronchioles or alveoli are present.</td>
</tr>
<tr>
<td>period</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canalicular</td>
<td>16 – 26 week</td>
<td>Each terminal bronchiole divides into 2 or more respiratory bronchioles, which in turn divide into 3-6 alveolar ducts. The cuboidal cells lining the respiratory bronchioles.</td>
</tr>
<tr>
<td>period</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Terminal sac</td>
<td>Up to birth</td>
<td>Cuboidal cells become very thin and flat and intimately associated with blood and lymph capillaries. Terminal sacs (primitive alveoli) form.</td>
</tr>
<tr>
<td>period</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alveolar period</td>
<td>Up to 10 years</td>
<td>Mature alveoli have well-developed epithelial endothelial (capillary) contacts.</td>
</tr>
</tbody>
</table>

Fetal Breathing movements begin before birth and:
- cause aspiration of amniotic fluid
- stimulate lung development and conditioning of respiratory muscles

At birth Lung fluid is reabsorb but not the surfactant coat. The surfactant prevents the collapse of the alveoli during expiration.

Growth of the lungs after birth is due to an increase in the number of respiratory bronchioles and alveoli and not an increase in size.
RESPIRATORY SYSTEM

The respiratory system (called also respiratory apparatus, ventilatory system) is a biological system consisting of specific organs and structures used for the process of respiration in an organism. The respiratory system is involved in the intake and exchange of oxygen and carbon dioxide between an organism and the environment.

In air-breathing vertebrates like human beings, respiration takes place in the respiratory organs called lungs. The passage of air into the lungs to supply the body with oxygen is known as inhalation, and the passage of air out of the lungs to expel carbon dioxide is known as exhalation; this process is collectively called breathing or ventilation.

In humans and other mammals, the anatomical features of the respiratory system include trachea, bronchi, bronchioles, lungs, and diaphragm. Molecules of oxygen and carbon dioxide are passively exchanged, by diffusion, between the gaseous external environment and the blood. This exchange process occurs in the alveoli (air sacs) in the lungs.

In fish and many invertebrates, respiration takes place through the gills. Other animals, such as insects, have respiratory systems with very simple anatomical features, and in amphibians even the skin plays a vital role in gas exchange. Plants also have respiratory systems but the directionality of gas exchange can be opposite to that in animals. The respiratory system in plants also includes anatomical features such as holes on the undersides of leaves known as stomata.

Comparative anatomy and physiology

Horses

Horses are obligate nasal breathers which means that they are different from many other mammals because they do not have the option of breathing through their mouths and must take in oxygen through their noses.
**Elephants**

The elephant is the only animal known to have no pleural space. Rather, the parietal and visceral pleura are both composed of dense connective tissue and joined to each other via loose connective tissue. This lack of a pleural space, along with an unusually thick diaphragm, are thought to be evolutionary adaptations allowing the elephant to remain underwater for long periods of time while breathing through its trunk which emerges as a snorkel.

**Birds**

The respiratory system of birds differs significantly from that found in mammals, containing unique anatomical features such as air sacs. The lungs of birds also do not have the capacity to inflate as birds lack a diaphragm and a pleural cavity. Gas exchange in birds occurs between air capillaries and blood capillaries, rather than in alveoli.

**Reptiles**

The anatomical structure of the lungs is less complex in reptiles than in mammals, with reptiles lacking the very extensive airway tree structure found in mammalian lungs. Gas exchange in reptiles still occurs in alveoli however, reptiles do not possess a diaphragm. Thus, breathing occurs via a change in the volume of the body cavity which is controlled by contraction of intercostal muscles in all reptiles except turtles. In turtles, contraction of specific pairs of flank muscles governs inspiration or expiration.

**Amphibians**

Both the lungs and the skin serve as respiratory organs in amphibians. The ventilation of the lungs in amphibians uses positive pressure ventilation. Muscles lower the floor of the oral cavity, enlarging it and drawing in air through the nostrils (which uses the same mechanics - pressure, volume, and diffusion - as a mammalian lung). With the nostrils and mouth closed, the floor of the oral cavity is forced up, which forces air down the trachea.
into the lungs. The skin of these animals is highly vascularized and moist, with moisture maintained via secretion of mucus from specialized cells. While the lungs are of primary importance to breathing control, the skin’s unique properties aid rapid gas exchange when amphibians are submerged in oxygen-rich water.

**Fish**

In most fish, respiration takes place through gills. Lungfish, however, do possess one or two lungs. The labyrinth fish have developed a special organ that allows them to take advantage of the oxygen of the air.

**Anatomy in invertebrates**

**Arthropods**

Some species of crab use a respiratory organ called a branchiostegal lung. Its gill tissue is formed so as to increase the surface area and the lung is more suited to taking oxygen from the air than from water. Some of the smallest spiders and mites can breathe simply by exchanging gas through the surface of the body. Larger spiders, scorpions and other arthropods use a primitive book lung.

**Insects**

Most insects breath passively through their spiracles (special openings in the exoskeleton) and the air reaches the body by means of a series of smaller and smaller pipes called ‘trachaea’ when their diameter is relatively large and ‘tracheoles’ when their diameter is very small. Diffusion of gases is effective over small distances but not over larger ones, this is one of the reasons insects are all relatively small. Insects which do not have spiracles and trachaea, such as some Collembola, breathe directly through their skins, also by diffusion of gases. The number of spiracles an insect has is variable between species, however they always come in pairs, one on each side of the body, and usually one per segment. Some of the Diplura have eleven, with four pairs on the thorax,
but in most of the ancient forms of insects, such as Dragonflies and Grasshoppers there are two thoracic and eight abdominal spiracles. However, in most of the remaining insects there are less. It is at this level of the tracheoles that oxygen is delivered to the cells for respiration. The trachea are water-filled due to the permeable membrane of the surrounding tissues. During exercise, the water level retracts due to the increase in concentration of lactic acid in the muscle cells. This lowers the water potential and the water is drawn back into the cells via osmosis and air is brought closer to the muscle cells. The diffusion pathway is then reduced and gases can be transferred more easily.

Insects were once believed to exchange gases with the environment continuously by the simple diffusion of gases into the tracheal system. More recently, however, large variation in insect ventilatory patterns have been documented and insect respiration appears to be highly variable. Some small insects do demonstrate continuous respiration and may lack muscular control of the spiracles. Others, however, utilize muscular contraction of the abdomen along with coordinated spiracle contraction and relaxation to generate cyclical gas exchange patterns and to reduce water loss into the atmosphere. The most extreme form of these patterns is termed discontinuous gas exchange cycles (DGC).

Molluscs

Molluscs generally possess gills that allow exchange of oxygen from an aqueous environment into the circulatory system. These animals also possess a heart that pumps blood which contains hemocyaninine as its oxygen-capturing molecule. Hence, this respiratory system is similar to that of vertebrate fish. The respiratory system of gastropods can include either gills or a lung.

Development

Humans and mammals

The respiratory system lies dormant in the human fetus during pregnancy. At birth, the respiratory system becomes fully functional
upon exposure to air, although some lung development and growth continues throughout childhood. Pre-term birth can lead to infants with under-developed lungs. These lungs show incomplete development of the alveolar type II cells, cells that produce surfactant. The lungs of pre-term infants may not function well because the lack of surfactant leads to increased surface tension within the alveoli. Thus, many alveoli collapse such that no gas exchange can occur within some or most regions of an infant’s lungs, a condition termed respiratory distress syndrome. Basic scientific experiments, carried out using cells from chicken lungs, support the potential for using steroids as a means of furthering development of type II alveolar cells. In fact, once a pre-mature birth is threatened, every effort is made to delay the birth, and a series of steroid shots is frequently administered to the mother during this delay in an effort to promote lung growth.

Disease

Disorders of the respiratory system can be classified into four general areas:

- Obstructive conditions (e.g., emphysema, bronchitis, asthma)
- Restrictive conditions (e.g., fibrosis, sarcoidosis, alveolar damage, pleural effusion)
- Vascular diseases (e.g., pulmonary edema, pulmonary embolism, pulmonary hypertension)
- Infectious, environmental and other “diseases” (e.g., pneumonia, tuberculosis, asbestosis, particulate pollutants):

Coughing is of major importance, as it is the body’s main method to remove dust, mucus, saliva, and other debris from the lungs. Inability to cough can lead to infection. Deep breathing exercises may help keep finer structures of the lungs clear from particulate matter, etc.

The respiratory tract is constantly exposed to microbes due to the extensive surface area, which is why the respiratory system
Development of the Respiratory System

includes many mechanisms to defend itself and prevent pathogens from entering the body.

Disorders of the respiratory system are usually treated internally by a pulmonologist and Respiratory Therapist.

Plants

Plants use carbon dioxide gas in the process of photosynthesis, and exhale oxygen gas as waste. The chemical equation of photosynthesis is \(6 \text{CO}_2\) (carbon dioxide) and \(6 \text{H}_2\text{O}\) (water) and that makes \(6 \text{O}_2\) (oxygen) and \(\text{C}_6\text{H}_{12}\text{O}_6\) (glucose). What is not expressed in the chemical equation is the capture of energy from sunlight which occurs. Photosynthesis uses electrons on the carbon atoms as the repository for that energy. Respiration is the opposite of photosynthesis. It reclaims the energy to power chemical reactions in cells. In so doing the carbon atoms and their electrons are combined with oxygen forming a gas which is easily removed from both the cells and the organism. Plants use both processes, photosynthesis to capture the energy and respiration to use it.

Plant respiration is limited by the process of diffusion. Plants take in carbon dioxide through holes on the undersides of their leaves known as stoma or pores. However, most plants require little air. Most plants have relatively few living cells outside of their surface because air (which is required for metabolic content) can penetrate only skin deep. However, most plants are not involved in highly aerobic activities, and thus have no need of these living cells.
The Neonatal Neuromechanical Unit

THE NEONATAL UNIT

The neonatal unit provides expert, round-the-clock care for newborn babies who are ill or born prematurely. If your baby is in the hospital’s neonatal unit, you are not alone. One in nine babies born in England will spend time on the neonatal unit.

There are different levels of care available on neonatal units. Depending on your baby’s needs, she will be in one of these units:

- Neonatal intensive care, for the most seriously ill babies.
- High-dependency care, for babies who do not need to be in the NICU but who still require complex care.
- Special care, for babies who are catching up on growth and development after a premature birth. These babies have less serious health problems or are getting better after more complex treatment.

There might also be transitional care. This happens just before your baby is ready to go home. Transitional care gives you a chance to take care of your baby yourself, but with the nurses nearby. Sometimes this means staying in a side room on the neonatal ward with your baby for a while.
Every hospital has a neonatal unit, but some may not be equipped to provide the level of care your baby needs. Your baby might therefore have to be transferred to a unit far from your home. This could also happen if your local hospital does not have enough room.

**My baby need to be in the neonatal unit**

Premature babies need extra help while their bodies catch up on the growth and development they missed in the uterus (womb). For example, it’s harder for your baby to stay warm because she can’t regulate her own body temperature yet. A special cot (incubator) can help with this.

If your baby is too small, weak or immature to feed, she might receive fluids and a nutrition mixture through a drip. Or she might need a tube that carries milk into her stomach.

Premature babies also need extra monitoring, treatment and care. They are vulnerable and can have serious health problems. Some of the common problems associated with premature birth are:

- breathing problems
- bleeding in the brain
- heart conditions
- gut and digestive disorders
- eye problems
- jaundice
- anaemia
- infections

In the neonatal unit, the nurses and doctors are always checking for the signs of any of these problems. They can treat your baby promptly if they need to.

**Care for my baby in the unit**

On the neonatal unit, a skilled team from different professions will care for your baby. Some of the people you may meet include:
• Staff and specialist neonatal nurses.
• The senior nurse in charge of the unit, called the sister or unit manager.
• Consultant paediatrician or neonatologist, who leads your baby’s care.
• Other specialist doctors, such as surgeons.
• Staff grade doctors.
• Junior doctors.
• Physiotherapists to help with your baby’s development.
• Radiographers, who take x-rays and scans.
• Dietitians who advise on nutrition.
• Pharmacists.
• Nursery nurses.
• A social worker to help you with family issues, financial worries, and support that might be needed after you take your baby home.

Last but not least, there’s you, the parents. You know your baby best and are always her most important carers. The professionals will recognise this and treat you as part of the team. They should encourage you to take an active part in your baby’s care, as far as possible.

As well as looking after your baby, neonatal units also try to help you, your partner and your baby’s brothers and sisters. This is called family-centred care.

Most hospitals have an open-doors policy and their neonatal units are open 24 hours a day for parents to visit. Others have more restricted visiting hours.

If you’re not at the hospital, you can call the neonatal unit any time, day or night. Always ask questions or talk to the staff about any worries you may have.

All those machines and tubes for

It can be scary to see your baby attached to all sorts of machines.
It can make you feel that you will never get the chance to be close to her. Be reassured that as your baby gets stronger, she will need fewer machines and it will be easier for you to hold her and care for her.

Some of these machines also have loud bleeping alarms and it can be frightening when they go off. Feel free to ask the nurses if you don’t know what an alarm means, and whether it’s anything serious.

Here is some of the equipment you could see in a neonatal unit:

**Baby warmers**

An incubator is a special cot that keeps your baby warm and sometimes controls the moisture level (humidity) around her. Some incubators have lids, some don’t. Some have overhead heaters.

**Monitors**

There are various monitors that help the neonatal unit’s team care for your baby.

Vital signs monitors are machines that might be used to keep track of your baby’s heart beat, breathing rate, blood pressure and temperature. Nurses will attach sticky pads to your baby’s chest. The pads are in turn attached to wires, which feed through electronic information to the monitor about how your baby is doing. The monitor alarms can sound off quite often.

Blood saturation monitors measures how much oxygen is in your baby’s blood. Sticky pads might be strapped to your baby’s foot or hand to feed information to the machine.

**Help with breathing**

A ventilator can help your baby’s lungs do the work of breathing. Your baby might need a ventilator if she is very premature or weak. The doctor will gently insert a tube into your baby’s windpipe. Via the tube, the ventilator feeds a mixture of
air and oxygen mixture into and out of your baby’s lungs, mimicking a breathing pattern.

A CPAP machine (the capitals stand for continuous positive airway pressure) is another piece of equipment that can help your baby breathe. A CPAP machine gently inflates your baby’s lungs and helps to keep them open. Air goes in through a mask or via a tube in your baby’s nose called a nasal cannula.

If your baby just needs extra oxygen, her incubator might have a see-through head box to help with this or she might receive oxygen through a mask or a nasal cannula.

**Tubes**

The unit’s team may place a fine needle attached to a tube in your baby’s veins to make sure she receives the fluids, medicines or nutrition she needs. The team may also insert tubes in her arteries to test her blood pressure, oxygen and carbon dioxide levels.

An infusion pump is a machine that makes sure that your baby receives her medicines and fluids via tubes at the right rate and speed.

A feeding (gastric) tube enables your baby to have milk fed straight into her tummy if she is not ready to feed from the breast or bottle. Nurses will gently insert a soft, flexible tube through your baby’s mouth or nose and down into her stomach.

**Special lights**

Phototherapy lights help your baby to recover if she has jaundice. Many newborns have jaundice. Their skin turns yellow because a substance called bilirubin builds up faster than their bodies can break it down.

Phototherapy lights helps your baby’s body to convert the bilirubin to a harmless substance until her body can do this by itself. The lights also convert the bilirubin to a form that is more easily excreted. Your baby is placed under the lights and wears a mask to protect her eyes.
About visiting my baby in the unit

Parents are usually allowed to be with their baby any time, day or night. Brothers and sisters are often encouraged to visit, too. Other people may be able to visit but not too many at once.

Generally speaking, it’s not a good idea for people with colds and flu to visit the unit. Ask one of the nurses about your unit’s policies.

How can I help my baby while she is in the unit?

Your premature baby needs all the things that other babies need from their parents. Your touch, your voice and your presence all help a great deal. There are many things you can do to help your baby while she is in the neonatal unit. Here are just some of them:

Kangaroo care

Once your baby is strong enough, one very good way to help her development is kangaroo care. You simply hold your baby inside your shirt, against your bare skin. Kangaroo care is soothing for your baby, and can improve her health and development.

In studies, kangaroo care has been shown to reduce infections, encourage breastfeeding and promote bonding. Staff on the unit can show you how to hold your baby when she is ready.

Feed your baby

As your baby gets stronger you can start feeding her, too. If you’re keen to breastfeed let the nurses know. They should make every effort to help you with this.

The nurses should help you to express your milk in the early days before your baby is strong enough to breastfeed. The expressed milk will be stored and used to feed her when she is ready.

Giving your premature baby breastmilk can encourage her brain development and help her to fight illness. Breastfed babies also go home from hospital sooner.
It’s not always easy to breastfeed when your baby is premature, for all sorts of reasons. It’s especially hard when you are stressed and worried about your baby. So do make sure that you get lots of help and support.

**Care for your baby**

It may take some time, but as your baby gets stronger you can start doing all those ordinary things that most parents take for granted, such as changing her nappy and giving her a bath.

**Speak up for your baby**

Like all parents, sometimes you have to speak up for your child and be their advocate. If you think something is wrong, trust your instincts. Talk to the staff. Don’t be afraid to ask questions and to voice your worries or concerns.

**Look after yourself**

One of the most important things you and your partner can do for your baby is look after yourselves.

Get some sleep, eat regular, balanced meals, and take a break from it all.

It’s exhausting having a baby in the neonatal unit, especially if you have other children or if you’re recovering from a difficult birth. It’s natural to put your baby first but be good to yourself, too.

**When can my baby come home?**

It’s hard to say because all babies are different. It depends on how your baby’s doing. Babies who are smaller and those born sooner tend to have more problems and so tend to stay longer on the unit.

A premature baby who is otherwise well usually stays in the neonatal unit until around the date she was due to be born. If your baby is doing really well, she might even be able to come home sooner than this.
COMMON CONDITIONS TREATED IN THE NEONATAL INTENSIVE CARE UNIT (NICU)

Premature babies and other very sick newborns face some of the same medical issues. Listed below are some medical conditions that may be seen in the neonatal intensive care unit (NICU).

The conditions listed may not be relevant to your baby’s situation. We encourage you to read only what you feel would be helpful to you and your child’s particular circumstances.

**Anemia**

Premature babies are often anemic. This means that they don’t have enough red blood cells. Normally, the fetus stores iron during the latter months of pregnancy and uses it after birth to make red blood cells. Infants born too soon may not have had enough time to store iron.

Loss of blood from frequent blood tests also can contribute to anemia. Anemic infants may be treated with dietary iron supplements, drugs that increase red blood cell production, or, in some cases, a blood transfusion.

**Breathing problems**

Premature babies often have breathing problems because their lungs aren’t fully developed. Full-term babies also can develop breathing problems due to complications of labor and delivery, birth defects, and infections. An infant with breathing problems may be given medicines, put on a respirator to help him breathe, or use a combination of these two treatments.

Apnea: Premature babies sometimes don’t breathe regularly. A baby may take a long breath, then a short one, then pause for five to 10 seconds before starting to breathe normally. This is called periodic breathing. It usually isn’t harmful, and the baby will outgrow it.

Premature and sick babies also may stop breathing for 15 to 20 seconds or more. This interruption in breathing is called apnea.
It may be accompanied by a slow heart rate called bradycardia. Babies in the NICU are constantly monitored for apnea and bradycardia (often called “A’s and B’s”).

Sensors on the baby’s chest send information about his breathing and heart rate to a machine located near the incubator. If a baby stops breathing, an alarm will begin beeping.

A nurse will stimulate the baby to start breathing by patting him or touching the soles of his feet. The neonatologist might consider giving the baby medicine or using equipment, such as continuous positive airway pressure (C-PAP), which is delivering air to a baby’s lungs through either small tubes in the baby’s nose or through a tube inserted into the windpipe).

Bronchopulmonary dysplasia (BPD): This chronic lung disease is most common in premature babies who have been treated for respiratory distress syndrome (RDS).

Babies with RDS have immature lungs. They sometimes need a mechanical ventilator to help them breathe. Some babies treated for RDS may develop symptoms of BPD, including fluid in the lungs, scarring, and lung damage.

Babies with BPD are treated with medications to make breathing easier. They’re slowly weaned from the ventilator. Their lungs usually improve over the first two years of life, but some children develop a chronic lung disease resembling asthma.

BPD also occasionally occurs in full-term newborns after they’ve had pneumonia or other infections.

Persistent pulmonary hypertension of the newborn (PPHN): Babies with PPHN cannot breathe properly because they have high blood pressure in their lungs. At birth, the blood vessels in the lungs normally relax in response to the first minutes of breathing air and allow blood to flow through them. This is how the blood picks up oxygen.

In babies with PPHN, this response doesn’t occur. This leads to a lack of oxygen in the blood, and sometimes to other complications including brain damage. Babies with PPHN often
have birth defects (such as heart defects) or have suffered from birth complications.

Babies with PPHN often need a ventilator (respirator) to help them breathe. They may be given a gas called nitric oxide through a tube in the windpipe. This treatment may help the blood vessels in the lungs relax and improve breathing.

Pneumonia: This lung infection is common in premature and sick newborns. A baby’s doctors may suspect pneumonia if the baby has difficulty breathing, if his rate of breathing changes, if blood tests happen to show low oxygen levels, or if the baby has an increased number of apnea episodes.

The doctor listens to the baby’s lungs with a stethoscope and then does an X-ray to see if there’s excess fluid in the lungs.

Sometimes the doctor may insert a tube into the lungs to take a sample of the lung fluid. The fluid is then tested to see what type of bacterium or virus is causing the infection, so that the doctor can choose the most effective drug to treat it.

Babies with pneumonia are generally treated with antibiotics. They also may need additional oxygen until the infection clears up.

Respiratory distress syndrome (RDS): Babies born before 34 weeks of pregnancy often develop this serious breathing problem. RDS is sometimes called hyaline membrane disease.

Babies with RDS lack a chemical mixture called surfactant, which keeps the small air sacs in the lungs from collapsing. Treatment with surfactant helps affected babies breathe more easily.

Babies with RDS also may receive a treatment called continuous positive airway pressure (C-PAP). The air may be delivered through small tubes inserted into the baby’s nose or windpipe.

As with surfactant treatment, C-PAP helps keep small air sacs from collapsing. C-PAP helps your baby breathe, but does not breathe for him. The sickest babies may temporarily need to be put on a ventilator while their lungs recover.
Congenital heart defects

These heart defects are present at birth. They originate in the early part of pregnancy when the heart is forming.

Bradycardia: Premature babies sometimes do not breathe regularly. Interrupted breathing, also called apnea, can cause bradycardia. This is an unhealthy, slow heart rate.

When they occur together, NICU staff call apnea and bradycardia “A’s and B’s.” Treatments include medicines and breathing support.

Coarctation of the aorta: The aorta is the large artery that sends blood from the heart to the rest of the body. In this condition, the aorta may be too narrow for the blood to flow evenly.

A surgeon can cut away the narrow part and sew the open ends together, replace the constricted section with manmade material, or patch it with part of a blood vessel taken from elsewhere in the body. Sometimes, this narrowed area can be widened by inflating a balloon on the tip of a catheter inserted through an artery.

Heart valve abnormalities: Some babies are born with heart valves that are narrowed, closed, or blocked, and this condition prevents blood from flowing smoothly. Some babies may need to have a shunt (artificial graft) placed to allow blood to bypass the blockage until the baby is big enough to have the valve repaired or replaced.

Patent ductus arteriosus (PDA): PDA is the most common heart problem in premature babies. Before birth, much of a fetus’s blood goes through a passageway (ductus arteriosus) from one blood vessel to another, instead of through the lungs. This is because the lungs aren’t yet in use.

This passageway should close soon after birth, so the blood can take the normal route from heart to lungs and back. If it doesn’t close, blood doesn’t flow correctly. In some cases, drug treatment can help close the passageway. If that doesn’t work, surgery can also close it.
Septal defects: A septal defect refers to a hole in the wall (septum) that divides the two upper or lower chambers of the heart. Because of this hole, the blood cannot circulate as it should, and the heart has to work extra hard.

A surgeon can close the hole by sewing or patching it. Small holes may heal by themselves and may not need repair at all.

Tetralogy of Fallot: In this condition, a combination of four heart defects keeps some blood from getting to the lungs. As a result, a baby’s skin can sometimes look blue from a lack of oxygen (cyanosis), and he may grow poorly. New surgical techniques allow this complex heart defect to be repaired early in life.

Transposition of the great arteries: In this condition, the positions of the two major arteries leaving the heart are reversed. Each artery arises from the wrong pumping chamber. Surgical advances have enabled correction of this defect in the newborn period.

**Feeding issues**

Experts agree that breast milk provides many wonderful and vital health benefits for newborns, especially premature or sick babies. A baby needs good nutrition to grow and become stronger. But he may need to be fed a different way for a while, before he is ready for the breast or a bottle.

Babies who are very small or sick are often fed through a vein (intravenously). A tiny needle is placed in a vein in the baby’s hand, foot, scalp, or belly button. He’ll receive sugar (glucose) and essential nutrients through the vein.

As soon as the baby is strong enough, he’ll be fed breast milk or formula through a tube placed through the nose or mouth into the stomach or intestines. This is called gavage feeding.

In gavage feeding, the tube may be left in place or inserted at each feeding. Inserting the tube shouldn’t bother the baby too much because babies this small generally don’t gag.
When the baby can suck and swallow effectively, gavage feedings will be stopped, and the baby will be able to breastfeed or bottle-feed.

Many babies in NICUs start trophic (minimal) feeds shortly after birth. This is done to stimulate the baby’s intestine until he’s strong enough to tolerate larger feedings.

Find out more about feeding your baby in the NICU.

**Gastrochisis**

This is a birth defect of the abdominal wall. The baby’s intestines, and sometimes other organs, are outside of the baby’s abdomen. Surgery is done to put the baby’s organs back in place and close the abdominal wall.

**Hypoglycemia**

Hypoglycemia is low blood sugar (glucose). It’s usually diagnosed in a baby shortly after birth. Babies born to mothers with diabetes have their glucose levels checked regularly to assess for hypoglycemia. Early feeding and an intravenous glucose solution help to prevent and treat hypoglycemia.

**Inability to control body heat**

Babies who are born too small and too soon often have trouble controlling their body temperature. Unlike healthy, full-term babies, they don’t have enough fat to prevent the loss of heat from their body.

Babies in the NICU are placed in an incubator or warmer right after birth to help control their temperature. A tiny thermometer taped to the baby’s stomach senses his body temperature and regulates the heat in the incubator. A baby will grow faster if he maintains a normal body temperature (98.6 degrees F.).

**Intrauterine growth restriction (IUGR)**

A baby with this condition grows more slowly than usual in utero, and is smaller than normal for his gestational age at birth.
IUGR is ordinarily diagnosed during pregnancy through an ultrasound. It usually is due to fetal or maternal complications. Upon admission to the NICU, babies are tested to determine possible causes, although this isn’t always able to be determined.

**Intraventricular hemorrhage (IVH)**

IVH refers to bleeding in the brain and is most common in the smallest premature babies (those weighing less than 3 1/3 pounds). The bleeds usually occur in the first four days of life.

Bleeding generally occurs near the fluid-filled spaces (ventricles) in the center of the brain. An ultrasound examination can show whether a baby has had a brain bleed and how severe it is.

Brain bleeds are usually given a number from 1 to 4, with 4 being the most severe. Most brain bleeds are mild (grades 1 and 2) and resolve themselves with no or few lasting problems.

More severe bleeds can cause difficulties for the baby during the hospitalization and possible complications in the future. Some will require careful monitoring of the baby’s development throughout infancy and childhood.

**Jaundice**

Babies with jaundice have a yellowish color to their skin and eyes. Jaundice occurs when the liver is too immature or sick to remove a waste product called bilirubin from the blood.

Bilirubin is formed when old red blood cells break down. Jaundice is especially common in premature babies and in babies who have blood type incompatibilities with their mothers (such as Rh disease, ABO incompatibility, or G6PD disease).

Jaundice itself doesn’t usually cause harm to a baby. But a very high bilirubin level can result in more serious problems, especially for premature babies.

For this reason, the baby’s bilirubin level is checked frequently. If it gets too high, he’s treated with special blue lights
(phototherapy) that help the body break down and eliminate bilirubin.

Occasionally, a baby will need a special type of blood transfusion called an exchange transfusion to reduce very high bilirubin levels. In this procedure, some of the baby’s blood is removed and replaced with blood from a donor.

**Macrosomia**

A condition in which a baby is born with excessive birth weight, that is, 4,500 grams (9 pounds, 14 ounces) or more. This is commonly due to maternal diabetes and may require delivery by cesarean section. These babies are also monitored for hypoglycemia.

**Necrotizing enterocolitis (NEC)**

This potentially dangerous intestinal problem most commonly affects premature babies. The bowel may become damaged when its blood supply is decreased. Bacteria that are normally present in the bowel invade the damaged area, causing more damage.

Babies with NEC develop feeding problems, abdominal swelling, and other complications. If tests show that a baby has NEC, he’ll be fed intravenously while his bowel heals. Sometimes damaged sections of intestine must be surgically removed.

**Retinopathy of prematurity (ROP)**

ROP is an abnormal growth of blood vessels in the eye. It occurs most often in babies born before 30 weeks of pregnancy.

ROP can lead to bleeding and scarring that can damage the eye’s retina (the lining at the rear of the eye that relays messages to the brain). This can result in vision loss.

An ophthalmologist (eye doctor) can examine the baby’s eyes for signs of ROP.

Most mild cases heal without treatment, with little or no vision loss. In more severe cases, the ophthalmologist may perform
laser therapy or do a procedure called cryotherapy (freezing) to eliminate abnormal blood vessels and scars. Both treatments help protect the retina.

**Sepsis**

Some babies are admitted to the NICU to determine whether they have this potentially dangerous infection of the bloodstream. The infection is caused by a germ that the baby has had difficulty fighting off.

Certain lab tests, cultures, and X-rays can help diagnose this condition. These tests may be recommended if your baby has symptoms such as temperature instability, high or low blood sugar levels, breathing problems, or low blood pressure.

The condition is treated with antibiotics, and the baby is monitored closely for an improvement in symptoms.
The purpose of the respiratory system is to perform gas exchange. Pulmonary ventilation provides air to the alveoli for this gas exchange process. At the respiratory membrane, where the alveolar and capillary walls meet, gases move across the membranes, with oxygen entering the bloodstream and carbon dioxide exiting. It is through this mechanism that blood is oxygenated and carbon dioxide, the waste product of cellular respiration, is removed from the body.

In order to understand the mechanisms of gas exchange in the lung, it is important to understand the underlying principles of gases and their behavior. In addition to Boyle’s law, several other gas laws help to describe the behavior of gases.

Gas Laws and Air Composition

Gas molecules exert force on the surfaces with which they are in contact; this force is called pressure. In natural systems, gases are normally present as a mixture of different types of molecules. For example, the atmosphere consists of oxygen, nitrogen, carbon dioxide, and other gaseous molecules, and this gaseous mixture exerts a certain pressure referred to as atmospheric pressure. Partial pressure (Px) is the pressure of a single type of gas in a mixture of gases. For example, in the atmosphere, oxygen exerts a partial pressure, and nitrogen exerts another partial pressure, independent
Basics of Gas Exchange

of the partial pressure of oxygen. Total pressure is the sum of all the partial pressures of a gaseous mixture. Dalton's law describes the behavior of nonreactive gases in a gaseous mixture and states that a specific gas type in a mixture exerts its own pressure; thus, the total pressure exerted by a mixture of gases is the sum of the partial pressures of the gases in the mixture.

**Partial and total pressure of a gas**

Partial pressure is the force exerted by a gas. The sum of the partial pressures of all the gases in a mixture equals the total pressure.

Partial pressure is extremely important in predicting the movement of gases. Recall that gases tend to equalize their pressure in two regions that are connected. A gas will move from an area where its partial pressure is higher to an area where its partial pressure is lower. In addition, the greater the partial pressure difference between the two areas, the more rapid is the movement of gases.

**Solubility of Gases in Liquids**

Henry's law describes the behavior of gases when they come into contact with a liquid, such as blood. Henry's law states that the concentration of gas in a liquid is directly proportional to the solubility and partial pressure of that gas. The greater the partial pressure of the gas, the greater the number of gas molecules that will dissolve in the liquid. The concentration of the gas in a liquid is also dependent on the solubility of the gas in the liquid. For example, although nitrogen is present in the atmosphere, very little nitrogen dissolves into the blood, because the solubility of nitrogen in blood is very low. The exception to this occurs in scuba divers; the composition of the compressed air that divers breathe causes nitrogen to have a higher partial pressure than normal, causing it to dissolve in the blood in greater amounts than normal. Too much nitrogen in the bloodstream results in a serious condition that can be fatal if not corrected. Gas molecules establish an
equilibrium between those molecules dissolved in liquid and those in air.

The composition of air in the atmosphere and in the alveoli differs. In both cases, the relative concentration of gases is nitrogen > oxygen > water vapor > carbon dioxide. The amount of water vapor present in alveolar air is greater than that in atmospheric air. Recall that the respiratory system works to humidify incoming air, thereby causing the air present in the alveoli to have a greater amount of water vapor than atmospheric air. In addition, alveolar air contains a greater amount of carbon dioxide and less oxygen than atmospheric air. This is no surprise, as gas exchange removes oxygen from and adds carbon dioxide to alveolar air. Both deep and forced breathing cause the alveolar air composition to be changed more rapidly than during quiet breathing. As a result, the partial pressures of oxygen and carbon dioxide change, affecting the diffusion process that moves these materials across the membrane. This will cause oxygen to enter and carbon dioxide to leave the blood more quickly.

**Ventilation and Perfusion**

Two important aspects of gas exchange in the lung are ventilation and perfusion. Ventilation is the movement of air into and out of the lungs, and perfusion is the flow of blood in the pulmonary capillaries. For gas exchange to be efficient, the volumes involved in ventilation and perfusion should be compatible. However, factors such as regional gravity effects on blood, blocked alveolar ducts, or disease can cause ventilation and perfusion to be imbalanced.

**GAS EXCHANGE**

Gas exchange is a biological process through which different gases are transferred in opposite directions across a specialized respiratory surface. Gases are constantly required by, and produced as a by-product of, cellular and metabolic reactions, so an efficient system for their exchange is extremely important. It is linked with
respiration in animals, and both respiration and photosynthesis in plants.

In respiration, oxygen (O\textsubscript{2}) is required to enter cells, while waste carbon dioxide (CO\textsubscript{2}) must be excreted; the opposite is true for photosynthesis, in which CO\textsubscript{2} enters plants and O\textsubscript{2} is released. The exchange of gases essentially occurs as a result of diffusion down a concentration gradient: gas molecules moving from an area of high concentration to low concentration.

**Diffusion**

Diffusion follows Fick’s Law. It is a passive process (no energy is required) affected by factors such as the surface area available, the distance the gas molecules must diffuse across and the concentration gradient.

Gases must first dissolve in a liquid in order to diffuse across a membrane, so all gas exchange systems require a moist environment.

In single-celled organisms, diffusion can occur straight across the cell membrane; as organisms increase in size, so does the distance gases must travel across. (Their surface area-to-volume ratio also decreases.) Diffusion alone is not efficient enough and specialized respiratory systems are required. This is the case with humans and with fish that have evolved circulatory systems: these are able to transport the gases to and from the respiratory surface and maintain a continuous concentration gradient.

**In humans**

Both oxygen and carbon dioxide are transported around the body in the blood through arteries, veins and capillaries. They bind to haemoglobin in red blood cells, although oxygen does so more effectively. Carbon dioxide also dissolves in the plasma or combines with water to form bicarbonate ions (HCO\textsuperscript{−}\textsubscript{3}). This reaction is catalyzed by the carbonic anhydrase enzyme in red blood cells.
The main respiratory surface in humans is the alveoli, which are small air sacs branching off from the bronchioles in the lungs. They are one cell thick and provide a moist and extremely large surface area for gas exchange to occur. Capillaries carrying deoxygenated blood from the pulmonary artery run across the alveoli. They are also extremely thin, so the total distance gases must diffuse across is only around 2 cells thick. An adult male has about 300 million alveoli, each ranging in diameter from 75 to 300 µm.

Inhaled oxygen is able to diffuse into the capillaries from the alveoli, while \( \text{CO}_2 \) from the blood diffuses in the opposite direction into the alveoli. The waste \( \text{CO}_2 \) can then be exhaled out of the body. Continuous blood flow in the capillaries and constant breathing maintain a steep concentration gradient.

**Varying response**

During physical exercise, excess carbon dioxide is produced as a result of increased respiration, and muscles and cells require increased oxygen. The body responds to this change by increasing the breathing rate, maximizing the rate of possible gas exchange.

**In plants**

Gas exchange in plants is dominated by the roles of carbon dioxide and water vapor. \( \text{CO}_2 \) is the only carbon source for autotrophic organisms, making it essential for the conversion of light into sugar during photosynthesis. Due to the high differences in water potential in the plant versus the surrounding air, water vapor tends to evaporate from plants. Gas exchange is mediated through pores (known as stomata and located mainly on the lower side of leaves) that underlie a complex regulatory system. As the condition of the stomata unavoidably influences both the \( \text{CO}_2 \) and water vapor exchanges, plants experience a gas exchange dilemma: gaining enough \( \text{CO}_2 \) without losing too much water.

Gas exchange measurements are common tools in plant science. If the environmental conditions (humidity, \( \text{CO}_2 \) concentration,
light and temperature) are fully controlled, the measurements of CO₂ uptake and water release reveal important information about the CO₂ assimilation and transpiration rates and the intercellular CO₂ concentration, which reveal important information about the photosynthetic condition of the plants.

Oxygen, essential for respiration during the night, plays a minor role in plants’ gas exchange as it is always present in sufficient amounts.

**GAS EXCHANGE - ANATOMY & PHYSIOLOGY**

The air in the alveoli is renewed regularly, thanks to the ventilation process. Gas exchange in the lungs takes place between the blood in the capillary network surrounding the alveoli, and the air in the alveoli itself.

All of the blood from the right ventricle flows through the pulmonary artery to the capillary network which surrounds the alveoli. Another set of pulmonary capillaries receive small amounts of arterial blood from the left ventricle, via the bronchial arteries. These capillaries provide oxygen and nutrients to the lung tissue.

**Principles of Gaseous Exchange**

Gas exchange between the air within the alveoli and the pulmonary capillaries occurs by **diffusion**. The oxygen must first dissolve before passing through the respiratory epithelium. Gas moves from a region of high partial pressure to a region of low partial pressure, down a partial pressure gradient. Partial pressure is a term used to measure gases. ‘P’ is the symbol used for this term. The distance between the air within the alveoli, and the blood is approx 0.7 micrometers. This distance is decreased during inhalation as the lung distends. This tiny distance allows extremely fast and efficient diffusion.

**Oxygen**

The PO₂ is always lower in the alveoli compared to the external environment due to the oxygen diffusing across the alveolar wall.
continuously, and the CO\textsubscript{2} entering the alveoli which has the effect of ‘diluting’ the oxygen, as it is travelling in the opposite direction to the O\textsubscript{2}. The PO\textsubscript{2} in the alveoli is still higher than that in the capillaries, so oxygen diffuses into the blood. Once through the alveolar and capillary walls, the oxygen combines with haemoglobin to form oxyhaemoglobin and is transported within the bloodstream.

**Carbon Dioxide**

Carbon dioxide enters the red blood cell as a waste product from cells. In the red blood cell it reacts with water to form carbonic acid, CA. CA dissociates to bicarbonate ions and hydrogen ions. These diffuse into plasma, where H are buffered by haemoglobin. Approx 5% of the total body CO\textsubscript{2} dissolves in the plasma, approx 5% of the total body CO\textsubscript{2} is carried as carboxyhaemoglobin on proteins and approx 90% is carried as bicarbonate ions in the plasma. The PCO\textsubscript{2} in the capillaries is higher than that in the alveoli, thus CO\textsubscript{2} diffuses into the alveoli, where it is exhaled.

**V-Q Ratio**

The adequacy of pulmonary gas exchange relies on the V-Q ratio. The alveoli should receive the ideal amounts of blood and gas for gas exchange.

In disease situations, the amount of air delivered may be reduced, the alveolar wall may be thickened or the alveolar surface area may be reduced meaning that less gas is able to diffuse out of the alveolus. Alternatively, blood supply may be impaired so that despite sufficient ventilation, insufficient exchange occurs to support the body.

**Species Differences**

Terrestrial vertebrates also have the ability to undergo gas exchange within their skin, as well as the lungs. This may account to 2% of the total gas exchange occurring within the body. This is important during its thermoregulatory functions, which involves
Basics of Gas Exchange

reduced cutaneous circulation when cold temperatures are experienced.

MECHANISMS FOR GAS EXCHANGE

All living things obtain the energy they need by metabolizing energy-rich compounds, such as carbohydrates and fats. In the majority of organisms, this metabolism takes place by respiration, a process that requires oxygen. In the process, carbon dioxide gas is produced and must be removed from the body.

In plant cells, carbon dioxide may appear to be a waste product of respiration, too, but because it is used in photosynthesis, carbon dioxide may be considered a by-product. Carbon dioxide must be available to plant cells, and oxygen gas must be removed. Gas exchange is thus an essential process in energy metabolism, and gas exchange is an essential prerequisite to life, because where energy is lacking, life cannot continue.

The basic mechanism of gas exchange is diffusion across a moist membrane. Diffusion is the movement of molecules from a region of greater concentration to a region of lesser concentration, in the direction following the concentration gradient. In living systems, the molecules move across cell membranes, which are continuously moistened by fluid.

Simple organisms

Single-celled organisms, such as bacteria and protozoa, are in constant contact with their external environment. Gas exchange occurs by diffusion across their membranes. Even in simple multicellular organisms, such as green algae, their cells may be close to the environment, and gas exchange can occur easily.

In larger organisms, adaptations bring the environment closer to the cells. Liverworts, for instance, have numerous air chambers in the internal environment. Sponges and hydras have water-filled central cavities, and planaria have branches of their gastrovascular cavity that connect with all parts of the body.
Plants

Although plants are complex organisms, they exchange their gases with the environment in a rather straightforward way. In aquatic plants, water passes among the tissues and provides the medium for gas exchange. In terrestrial plants, air enters the tissues, and the gases diffuse into the moisture bathing the internal cells.

In the leaf of the plant, an abundant supply of carbon dioxide must be present, and oxygen from photosynthesis must be removed. Gases do not pass through the cuticle of the leaf; they pass through pores called stomata in the cuticle and epidermis.

Stomata are abundant on the lower surface of the leaf, and they normally open during the day when the rate of photosynthesis is highest. Physiological changes in the surrounding guard cells account for the opening and closing of the stomata.

Animals

In animals, gas exchange follows the same general pattern as in plants. Oxygen and carbon dioxide move by diffusion across moist membranes. In simple animals, the exchange occurs directly with the environment.

But with complex animals, such as mammals, the exchange occurs between the environment and the blood. The blood then carries oxygen to deeply embedded cells and transports carbon dioxide out to where it can be removed from the body.

Earthworms exchange oxygen and carbon dioxide directly through their skin. The oxygen diffuses into tiny blood vessels in the skin surface, where it combines with the red pigment hemoglobin. Hemoglobin binds loosely to oxygen and carries it through the animal’s bloodstream. Carbon dioxide is transported back to the skin by the hemoglobin.

Terrestrial arthropods have a series of openings called spiracles at the body surface. Spiracles open into tiny air tubes called tracheae, which expand into fine branches that extend into all parts of the arthropod body.
Fish use outward extensions of their body surface called gills for gas exchange. Gills are flaps of tissue richly supplied with blood vessels. As a fish swims, it draws water into its mouth and across the gills. Oxygen diffuses out of the water into the blood vessels of the gill, while carbon dioxide leaves the blood vessels and enters the water passing by the gills.

Terrestrial vertebrates such as amphibians, reptiles, birds, and mammals have well-developed respiratory systems with lungs. Frogs swallow air into their lungs, where oxygen diffuses into the blood to join with hemoglobin in the red blood cells. Amphibians can also exchange gases through their skin. Reptiles have folded lungs to provide increased surface area for gas exchange. Rib muscles assist lung expansion and protect the lungs from injury.

Birds have large air spaces called air sacs in their lungs. When a bird inhales, its rib cage spreads apart and a partial vacuum is created in the lungs. Air rushes into the lungs and then into the air sacs, where most of the gas exchange occurs. This system is birds' adaptation to the rigors of flight and their extensive metabolic demands.

The lungs of mammals are divided into millions of microscopic air sacs called alveoli (the singular is alveolus). Each alveolus is surrounded by a rich network of blood vessels for transporting gases. In addition, mammals have a dome-shaped diaphragm that separates the thorax from the abdomen, providing a separate chest cavity for breathing and pumping blood. During inhalation, the diaphragm contracts and flattens to create a partial vacuum in the lungs. The lungs fill with air, and gas exchange follows.

**GASEOUS EXCHANGE IN THE LUNGS**

To supply the cells of our body with a continuous supply of oxygen for respiration and to remove the carbon dioxide generated by respiration, we have evolved a specialised exchange surface for gas exchange within the breathing system. The efficiency of this system is further improved by ventilation of this exchange surface.
and by having an efficient blood supply - both of which maintain a suitable concentration gradient.

**The lungs**

The lungs are part of the breathing system which is adapted for two functions:

- ventilation – the movement of air into and out of the lungs
- gas exchange – the ‘swapping’ of gases between the alveolar air and the blood

The lungs are located within the upper part of your body called the thorax. They are surrounded by the ribcage (which protects them) and in between the ribs are intercostal muscles which play a role in ventilating the lungs.

Beneath the lungs is a muscular sheet called the diaphragm. This separates the lungs from the abdomen of the body and also plays a role in ventilating the lungs.

Within the lungs is a network of tubes through which air is able to pass. Air is firstly warmed, moistened and filtered as it travels through the mouth and nasal passages. It then passes through the trachea and down one of the two bronchi and into one of the lungs.
After travelling into the many bronchioles, it finally passes into some of the millions of tiny sacs called alveoli, which have the specialised surfaces for gas exchange.

**Ventilation**

When you inhale:
1. The intercostal muscles contract, expanding the ribcage outwards and upwards.
2. The diaphragm contracts, pulling downwards to increase the volume of the chest.
3. Pressure inside the chest is lowered and air is sucked into the lungs.

When you exhale:
1. The intercostal muscles relax, the ribcage drops inwards and downwards.
2. The diaphragm relaxes, moving back upwards, decreasing the volume of the chest.
3. Pressure inside the chest increases and air is forced out.

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**Mechanical ventilation**

When a person stops breathing on their own, mechanical ventilation can be used until the patient is able to recover and again breathe independently. This is done by machines called ventilators - which fall into two main types:

1. Negative pressure ventilators - the patient is placed in an airtight machine from the neck down, and a vacuum is created around the thorax. This creates a negative pressure, which leads to the expansion of the thorax and a decrease in pressure. As a result, air is drawn into the lungs. As the vacuum is released, the elasticity of the lungs, diaphragm and chest wall cause exhalation.
2. Positive pressure ventilators - air is forced into the lungs through a tube which is inserted into the trachea. As the ventilator pumps air in, the lungs inflate. When the ventilator stops, the elasticity of the lungs, diaphragm and chest wall cause exhalation.

**Gas exchange**

Within the alveoli, an exchange of gases takes place between the gases inside the alveoli and the blood.

Blood arriving in the alveoli has a higher carbon dioxide concentration which is produced during respiration by the body’s cells. However, the air in the alveoli has a much lower concentration of carbon dioxide, meaning there is a concentration gradient which allows carbon dioxide to diffuse out of the blood and into the alveolar air.

Similarly, blood arriving in the alveoli has a lower oxygen concentration (as it has been used for respiration by the body’s cells), while the air in the alveoli has a higher oxygen concentration. Therefore, oxygen moves into the blood by diffusion and combines with the haemoglobin in red blood cells to form oxyhaemoglobin.

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This table shows the differences (approximate figures) in the composition of inhaled and exhaled air.
Basics of Gas Exchange

<table>
<thead>
<tr>
<th>Gas</th>
<th>% of inhaled air</th>
<th>% of exhaled air</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen</td>
<td>21</td>
<td>16</td>
</tr>
<tr>
<td>Carbon dioxide</td>
<td>0.04</td>
<td>4</td>
</tr>
<tr>
<td>Nitrogen</td>
<td>79</td>
<td>79</td>
</tr>
</tbody>
</table>

Adaptations of the alveoli

To maximise the efficiency of gas exchange, the alveoli have several adaptations:

- They are folded, providing a much greater surface area for gas exchange to occur.
- The walls of the alveoli are only one cell thick. This makes the exchange surface very thin - shortening the diffusion distance across which gases have to move.
- Each alveolus is surrounded by blood capillaries which ensure a good blood supply. This is important as the blood is constantly taking oxygen away and bringing in more carbon dioxide - which helps to maintain the maximum concentration gradient between the blood and the air in the alveoli.
- Each alveolus is ventilated, removing waste carbon dioxide and replenishing oxygen levels in the alveolar air. This also helps to maintain the maximum concentration gradient between the blood and the air in the alveoli.
VENTILATOR BASICS

Once the trachea has been successfully intubated and proper endotracheal tube placement has been verified by clinical and radiographic means, ventilator settings must be selected. The first parameter to be chosen is the ventilator mode. The mode determines how the ventilator initiates a breath, how the breath is delivered, and when the breath is terminated. Despite the availability of several new modes of ventilator support, time-tested modes such as assist-control (AC), synchronized intermittent mandatory ventilation (SIMV), and pressure support ventilation (PSV) are the most commonly used and the focus of this review.

Assist-control

Assist-control is a commonly used mode of mechanical ventilation in medical intensive care units. A key concept in the AC mode is that the tidal volume (\(V_T\)) of each delivered breath is the same, regardless of whether it was triggered by the patient or the ventilator. At the start of a cycle, the ventilator senses a patient’s attempt at inhalation by detecting negative airway
pressure or inspiratory flow. The pressure or flow threshold needed to trigger a breath is generally set by the respiratory therapist and is termed the trigger sensitivity. If the patient does not initiate a breath before a requisite period of time determined by the set respiratory rate (RR), the ventilator will deliver the set $V_T$. For example, if RR is set at 12 breaths per minute and the patient is not initiating breaths, the ventilator will deliver a breath every 5 seconds; this is called time-triggering. Similarly, if RR is 15 breaths per minute, the ventilator will deliver a breath every 4 seconds. However, if the patient initiates a breath, the ventilator in AC mode will deliver the set $V_T$; these breaths are patient-triggered rather than time-triggered.

Regardless of whether the breath is patient-triggered or time-triggered, the exhalation valve closes and the ventilator generates inspiratory flow at a set rate and pattern. The patient is limited to that flow rate and pattern during inhalation. Flow may be either constant (square waveform) or decelerating (ramp waveform). A square waveform is generally selected when inspiratory time is to be minimized thus allowing more time for exhalation (ie obstructive lung diseases). Ramp waveforms are useful for ventilating a heterogeneous lung, such as in the acute respiratory distress syndrome (ARDS). Often the flow rate and pattern are selected to maximize patient comfort and patient-ventilator synchrony. Inspiratory flow lasts until the set $V_T$ is delivered at which time the breath is cycled-off (and so the term volume-cycled mechanical ventilation).

Thus, the AC mode is patient- or time-triggered, flow-limited, and volume-cycled. An important correlate to this mode is that the airway pressures generated by chosen ventilator settings are determined by the compliance of the respiratory system and the resistance of the airways.

When the exhalation valve opens, the patient is allowed to exhale passively or actively until the airway pressure reaches end-expiratory pressure. This pressure is typically set slightly higher than atmospheric pressure to prevent atelectasis, decrease
inspiratory work of breathing, or improve gas exchange depending on the clinical scenario. This positive end-expiratory pressure (PEEP) is generated by a resistor in the exhalation port of the ventilator.

AC mode has several advantages including low work of breathing, as every breath is supported and tidal volume is guaranteed. However, there is concern that tachypnea could lead to hyperventilation and respiratory alkalosis. Breath stacking can occur when the patient initiates a second breath before exhaling the first. The results are high volumes and pressures in the system. Hyperventilation and breath stacking can usually be overcome by choosing optimal ventilator settings and appropriate sedation.

Synchronized Intermittent Mandatory Ventilation

Synchronized intermittent mandatory ventilation (SIMV) is another commonly used mode of mechanical ventilation. Like AC, SIMV delivers a minimum number of fully assisted breaths per minute that are synchronized with the patient’s respiratory effort. These breaths are patient- or time-triggered, flow-limited, and volume-cycled. However, any breaths taken between volume-cycled breaths are not assisted; the volumes of these breaths are determined by the patient’s strength, effort, and lung mechanics. A key concept is that ventilator-assisted breaths are different than spontaneous breaths. Another important concept is that AC and SIMV are identical modes in patients who are not spontaneously breathing due to heavy sedation or paralysis. High respiratory rates on SIMV allow little time for spontaneous breathing (a strategy very similar to AC), whereas low respiratory rates allow for just the opposite.

SIMV has been purported to allow the patient to exercise their respiratory musculature while on the ventilator by allowing spontaneous breaths and less ventilator support. However, SIMV may increase work of breathing and cause respiratory muscle fatigue that may thwart weaning and extubation.
Pressure Support Ventilation

A common strategy is to combine SIMV with an additional ventilator mode known as pressure support ventilation (PSV). In this situation, inspiratory pressure is added to spontaneous breaths to overcome the resistance of the endotracheal tube or to increase the volume of spontaneous breaths. PSV may also be used as a stand-alone mode to facilitate spontaneous breathing.

PSV mode is patient-triggered, pressure-limited, and flow-cycled. With this strategy, breaths are assisted by a set inspiratory pressure that is delivered until inspiratory flow drops below a set threshold. When added to SIMV, PSV is applied only to the spontaneous breaths taken between volume-guaranteed (volume-cycled) breaths.

During PSV alone, all breaths are spontaneous. Airway pressures drop to the set level of PEEP during exhalation and rise by the amount of selected pressure support during inhalation. RR and $V_T$ are determined by the patient; there is no set RR or $V_T$.

MODES OF MECHANICAL VENTILATION

Modes of mechanical ventilation are one of the most important aspects of the usage of mechanical ventilation. The mode refers to the method of inspiratory support. In general, mode selection is based on clinician familiarity and institutional preferences, since there is a paucity of evidence indicating that the mode affects clinical outcome.

The most frequently used forms of volume-limited mechanical ventilation are intermittent mandatory ventilation (IMV) and continuous mandatory ventilation (CMV). There have been substantial changes in the nomenclature of mechanical ventilation over the years, but more recently it has become standardized by many respirology and pulmonology groups. Writing a mode is most proper in all capital letters with a dash between the cycle and the strategy (i.e. PC-IMV, or VC-MMV etc.)
TAXONOMY FOR MECHANICAL VENTILATION

The taxonomy is a logical classification system based on 10 maxims of ventilator design 10 maxims.

A breath is one cycle of positive flow (inspiration) and negative flow (expiration) defined in terms of the flow-time curve. Inspiratory time is defined as the period from the start of positive flow to the start of negative flow. Expiratory time is defined as the period from the start of expiratory flow to the start of inspiratory flow. The flow-time curve is the basis for many variables related to ventilator settings.

A breath is assisted if the ventilator does work on the patient. An assisted breath is one for which the ventilator does some portion of the work of breathing. For constant flow inflation, work is defined as inspiratory pressure multiplied by tidal volume. Therefore, an assisted breath is identified as a breath for which airway pressure (displayed on the ventilator) rises above baseline during inspiration. An unassisted breath is one for which the ventilator simply provides the inspiratory flow demanded by the patient and pressure stays constant throughout the breath.

A ventilator assists breathing using either pressure control or volume control based on the equation of motion for the respiratory system. Providing assistance means doing work on the patient, which is accomplished by controlling either pressure or volume. A simple mathematical model describing this fact is known as the equation of motion for the passive respiratory system:

\[ \text{Pressure} = (\text{Elastance} \times \text{Volume}) + (\text{Resistance} \times \text{Flow}) \]

In this equation, pressure, volume, and flow are all continuous functions of time. Pressure is actually a pressure difference across the system (e.g., transrespiratory pressure defined as pressure at the airway opening minus pressure on the body surface). Elastance (defined as the change in pressure divided by the associated change in volume; the reciprocal of compliance) and resistance (defined as a change in pressure divided by the associated change in flow) are parameters assumed to remain constant during a breath.
Volume control (VC) means that both volume and flow are preset prior to inspiration. In other words, the right hand side of the equation of motion remains constant while pressure changes with changes in elastance and resistance.

Pressure control (PC) means that inspiratory pressure is preset as either a constant value or it is proportional to the patient’s inspiratory effort. In other words, the left-hand side of the equation of motion remains constant while volume and flow change with changes in elastance and resistance.

Time control (TC) means that, in some rare situations, none of the main variables (pressure, volume, or flow) are preset. In this case only the inspiratory and expiratory times are preset.

Breaths are classified by the criteria that trigger (start) and cycle (stop) inspiration. The start of inspiration is called the trigger event. The end of inspiration is called the cycle event.

Trigger and cycle events can be initiated by the patient or the machine. Inspiration can be patient triggered or patient cycled by a signal representing inspiratory effort. Inspiration may also be machine triggered or machine cycled by preset ventilator thresholds.

Patient triggering means starting inspiration based on a patient signal independent of a machine trigger signal. Machine triggering means starting inspiratory flow based on a signal from the ventilator, independent of a patient trigger signal. Patient cycling means ending inspiratory time based on signals representing the patient determined components of the equation of motion, (ie, elastance or resistance and including effects due to inspiratory effort). Flow cycling is a form of patient cycling because the rate of flow decay to the cycle threshold is determined by patient mechanics. Machine cycling means ending inspiratory time independent of signals representing the patient determined components of the equation of motion.

Breaths are classified as spontaneous or mandatory based on both the trigger and cycle events. A spontaneous breath is a breath
for which the patient both triggers and cycles the breath. A spontaneous breath may occur during a mandatory breath (e.g. Airway Pressure Release Ventilation). A spontaneous breath may be assisted or unassisted. A mandatory breath is a breath for which the machine triggers and/or cycles the breath. A mandatory breath can occur during a spontaneous breath (e.g., High Frequency Jet Ventilation). A mandatory breath is, by definition, assisted.

There are 3 breath sequences: Continuous mandatory ventilation (CMV), Intermittent Mandatory Ventilation (IMV), and Continuous Spontaneous Ventilation (CSV). A breath sequence is a particular pattern of spontaneous and/or mandatory breaths. The 3 possible breath sequences are: continuous mandatory ventilation, (CMV, spontaneous breaths are not allowed between mandatory breaths), intermittent mandatory ventilation (IMV, spontaneous breaths may occur between mandatory breaths), and continuous spontaneous ventilation (CSV, all breaths are spontaneous).

There are 5 basic ventilatory patterns: VC-CMV, VC-IMV, PC-CMV, PC-IMV, and PC-CSV. The combination VC-CSV is not possible because volume control implies machine cycling and machine cycling makes every breath mandatory, not spontaneous. A sixth pattern, TC-IMV is possible but rare.

Within each ventilatory pattern there are several variations that can be distinguished by their targeting scheme(s). A targeting scheme is a description of how the ventilator achieves preset targets. A target is a predetermined goal of ventilator output. Examples of within-breath targets include inspiratory flow or pressure and rise time (set-point targeting), tidal volume (dual targeting) and constant of proportionality between inspiratory pressure and patient effort (servo targeting). Examples of between-breath targets and targeting schemes include average tidal volume (for adaptive targeting), percent minute ventilation (for optimal targeting) and combined PCO2, volume, and frequency values describing a “zone of comfort” (for intelligent targeting, e.g., SmartCarePS or IntelliVent-ASV). The targeting scheme (or
combination of targeting schemes) is what distinguishes one ventilatory pattern from another. There are 7 basic targeting schemes that comprise the wide variety seen in different modes of ventilation:

Set-point: A targeting scheme for which the operator sets all the parameters of the pressure waveform (pressure control modes) or volume and flow waveforms (volume control modes).

Dual: A targeting scheme that allows the ventilator to switch between volume control and pressure control during a single inspiration.

Bio-variable: A targeting scheme that allows the ventilator to automatically set the inspiratory pressure or tidal volume randomly to mimic the variability observed during normal breathing.

Servo: A targeting scheme for which inspiratory pressure is proportional to inspiratory effort.

Adaptive: A targeting scheme that allows the ventilator to automatically set one target (eg, pressure within a breath) to achieve another target (eg, average tidal volume over several breaths).

Optimal: A targeting scheme that automatically adjusts the targets of the ventilatory pattern to either minimize or maximize some overall performance characteristic (eg, minimize the work rate done by the ventilatory pattern).

Intelligent: A targeting scheme that uses artificial intelligence programs such as fuzzy logic, rule based expert systems, and artificial neural networks.

A mode of ventilation is classified according to its control variable, breath sequence, and targeting scheme(s). The preceding 9 maxims create a theoretical foundation for a taxonomy of mechanical ventilation. The taxonomy is based on these theoretical constructs and has 4 hierarchical levels:

• Control Variable (Pressure or Volume, for the primary breath)
• Breath Sequence (CMV, IMV, or CSV)
• Primary Breath Targeting Scheme (for CMV or CSV)
• Secondary Breath Targeting Scheme (for IMV)

The “primary breath” is either the only breath there is (mandatory for CMV and spontaneous for CSV) or it is the mandatory breath in IMV. The targeting schemes can be represented by single, lower case letters: set-point = s, dual = d, servo = r, bio-variable = b, adaptive = a, optimal = o, intelligent = i. A tag is an abbreviation for a mode classification, such as PC-IMVs,s. Compound tags are possible, eg, PC-IMVo,i.

How modes are classified

Step 1: Identify the primary breath control variable. If inspiration starts with a preset inspiratory pressure, or if pressure is proportional to inspiratory effort, then the control variable is pressure. If inspiration starts with a preset tidal volume and inspiratory flow, then the control variable is volume. If neither is true, the control variable is time.

Step 2: Identify the breath sequence. Determine whether trigger and cycle events are patient or machine determined. Then, use this information to determine the breath sequence.

Step 3: Identify the targeting schemes for the primary breaths and (if applicable) secondary breaths.

Example mode classification

Mode Name: A/C Volume Control (Covidien PB 840)
1. Inspiratory volume and flow are preset, so the control variable is volume.
2. Every breath is volume cycled, which is a form of machine cycling. Any breath for which inspiration is machine cycled is classified as a mandatory breath. Hence, the breath sequence is continuous mandatory ventilation.
3. The operator sets all the parameters of the volume and flow waveforms so the targeting scheme is set-point. Thus, the mode is classified as volume control continuous mandatory ventilation with set-point targeting (VC-CMVs).
Mode Name: SIMV Volume Control Plus (Covidien PB 840)

1. The operator sets the tidal volume but not the inspiratory flow. Because setting volume alone (like setting flow alone) is a necessary but not sufficient criterion for volume control, the control variable is pressure.

2. Spontaneous breaths are allowed between mandatory breaths so the breath sequence is IMV.

3. The ventilator adjusts inspiratory pressure between breaths to achieve an average preset tidal volume, so the targeting scheme is adaptive. The mode tag is PC-IMV_a,s.

DESCRIPTIONS OF COMMON MODES

Assist mode, control mode, and assist-control mode

A basic distinction in mechanical ventilation is whether each breath is initiated by the patient (assist mode) or by the machine (control mode). Dynamic hybrids of the two (assist-control modes) are also possible, and control mode without assist is now mostly obsolete.

Airway pressure release ventilation

Airway pressure release ventilation is a time-cycled alternant between two levels of positive airway pressure, with the main time on the high level and a brief expiratory release to facilitate ventilation.

Airway pressure release ventilation is usually utilized as a type of inverse ratio ventilation. The exhalation time \( T_{\text{low}} \) is shortened to usually less than one second to maintain alveoli inflation. In the basic sense, this is a continuous pressure with a brief release. APRV currently the most efficient conventional mode for lung protective ventilation.

Different perceptions of this mode may exist around the globe. While ‘APRV’ is common to users in North America, a very similar mode, biphasic positive airway pressure (BIPAP), was introduced in Europe. The term APRV has also been used in American journals
where, from the ventilation characteristics, BIPAP would have been perfectly good terminology. But BiPAP\textsuperscript{tm} is a trademark for a noninvasive ventilation mode in a specific ventilator (Respironics Inc.).

Other manufacturers have followed with their own brand names (BILEVEL, DUOPAP, BIVENT). Although similar in modality, these terms describe how a mode is intended to inflate the lung, rather than defining the characteristics of synchronization or the way spontaneous breathing efforts are supported.

Intermittent mandatory ventilation has not always had the synchronized feature, so the division of modes were understood to be SIMV (synchronized) vs IMV (not-synchronized).

Since the American Association for Respiratory Care established a nomenclature of mechanical ventilation the “synchronized” part of the title has been dropped and now there is only IMV.

**Mandatory minute ventilation**

Mandatory minute ventilation (MMV) allows spontaneous breathing with automatic adjustments of mandatory ventilation to the meet the patient’s preset minimum minute volume requirement. If the patient maintains the minute volume settings for $V_T \times f$, no mandatory breaths are delivered.

If the patient’s minute volume is insufficient, mandatory delivery of the preset tidal volume will occur until the minute volume is achieved.

The method for monitoring whether or not the patient is meeting the required minute ventilation ($V_{\text{req}}$) differs by ventilator brand and model, but, in general, there is a window of monitored time, and a smaller window checked against the larger window (i.e., in the Dräger Evita\textsuperscript{®} line of mechanical ventilators there is a moving 20-second window, and every 7 seconds the current tidal volume and rate are measured) to decide whether a mechanical breath is needed to maintain the minute ventilation.
Basics of Respiratory Support and Mechanical Ventilation

MMV is an optimal mode for weaning in neonatal and pediatric populations and has been shown to reduce long-term complications related to mechanical ventilation.

**Pressure-regulated volume control**

Pressure-regulated volume control is an IMV based mode. Pressure-regulated volume control utilizes pressure-limited, volume-targeted, time-cycled breaths that can be either ventilator- or patient-initiated.

The peak inspiratory pressure delivered by the ventilator is varied on a breath-to-breath basis to achieve a target tidal volume that is set by the clinician.

For example, if a target tidal volume of 500 mL is set but the ventilator delivers 600 mL, the next breath will be delivered with a lower inspiratory pressure to achieve a lower tidal volume.

Though PRVC is regarded as a hybrid mode because of its tidal-volume (VC) settings and pressure-limiting (PC) settings fundamentally PRVC is a pressure-control mode with adaptive targeting.

**Continuous positive airway pressure**

Continuous positive airway pressure (CPAP) is a non-invasive positive pressure mode of ventilation (NPPV). CPAP is a pressure applied at the end of exhalation to keep the alveoli open and not fully deflate.

This mechanism for maintaining inflated alveoli helps increase partial pressure of oxygen in arterial blood, an appropriate increase in CPAP increases the $\text{PaO}_2$.

**Bilevel positive airway pressure**

Bilevel positive airway pressure (BPAP) is a mode used during noninvasive positive pressure ventilation (NPPV).

First used in 1988 by Professor Benzer in Austria, it delivers a preset inspiratory positive airway pressure (IPAP) and expiratory
positive airway pressure (EPAP). BPAP can be described as a Continuous Positive Airway Pressure system with a time-cycled change of the applied CPAP level. CPAP, BPAP and other non-invasive ventilation modes have been shown to be effective management tools for chronic obstructive pulmonary disease and acute respiratory failure.

Often BPAP is incorrectly referred to as “BiPAP”. BiPAP® is the name of a portable ventilator manufactured by Respironics Corporation; it is just one of many ventilators that can deliver BPAP.

**High-frequency ventilation (Active)**

The term active refers to the ventilator’s forced expiratory system. In a HFV-A scenario, the ventilator uses pressure to apply an inspiratory breath and then applies an opposite pressure to force an expiratory breath.

In high-frequency oscillatory ventilation (sometimes abbreviated HFOV) the oscillation bellows and piston force positive pressure in and apply negative pressure to force an expiration.

**High-frequency ventilation (Passive)**

The term passive refers to the ventilator’s non-forced expiratory system.

In a HFV-P scenario, the ventilator uses pressure to apply an inspiratory breath and then returns to atmospheric pressure to allow for a passive expiration. This is seen in High-Frequency Jet Ventilation, sometimes abbreviated HFJV.

**Volume guarantee**

Volume guarantee an additional parameter available in many types of ventilators that allows the ventilator to change its inspiratory pressure setting to achieve a minimum tidal volume.

This is utilized most often in neonatal patients who need a pressure controlled mode with a consideration for volume control to minimize volutrauma.
SPONTANEOUS BREATHING AND SUPPORT SETTINGS

Positive-end expiratory pressure

Positive end expiratory pressure (PEEP) is pressure applied upon expiration. PEEP is applied using either a valve that is connected to the expiratory port and set manually or a valve managed internally by a mechanical ventilator.

PEEP is a pressure that an exhalation has to bypass, in effect causing alveoli to remain open and not fully deflate. This mechanism for maintaining inflated alveoli helps increase partial pressure of oxygen in arterial blood, and an increase in PEEP increases the PaO$_2$.

Pressure support

Pressure support is a spontaneous mode of ventilation also named Pressure Support Ventilation (PSV). The patient initiates every breath and the ventilator delivers support with the preset pressure value. With support from the ventilator, the patient also regulates their own respiratory rate and their tidal volume.

In Pressure Support, the set inspiratory pressure support level is kept constant and there is a decelerating flow. The patient triggers all breaths. If there is a change in the mechanical properties of the lung/thorax and patient effort, the delivered tidal volume will be affected. The user must then regulate the pressure support level to obtain desired ventilation. Pressure support improves oxygenation, ventilation and decreases work of breathing.

OTHER VENTILATION MODES AND STRATEGIES

Closed loop systems

Adaptive Support Ventilation

Adaptive Support Ventilation is the only commercially available closed-loop mode of mechanical ventilation to date that
uses “optimal targeting”. This targeting scheme was first described by Tehrani in 1991, and was designed to minimize the work rate of breathing, mimic natural breathing, stimulate spontaneous breathing, and reduce weaning time.

**Automatic Tube Compensation**

Automatic Tube Compensation (ATC) is the simplest example of a computer-controlled targeting system on a ventilator. It is a form of servo targeting.

The goal of ATC is to support the resistive work of breathing through the artificial airway.

**Neurally Adjusted Ventilatory Assist**

Neurally Adjusted Ventilatory Assist (NAVA) is adjusted by a computer (servo) and is similar to ATC but with more complex requirements for implementation.

In terms of patient-ventilator synchrony, NAVA supports both resistive and elastic work of breathing in proportion to the patient’s inspiratory effort.

**Proportional Assist Ventilation**

Proportional assist ventilation (PAV) is another servo targeting based mode in which the ventilator guarantees the percentage of work regardless of changes in pulmonary compliance and resistance.

The ventilator varies the tidal volume and pressure based on the patient’s work of breathing. The amount it delivers is proportional to the percentage of assistance it is set to give.

PAV, like NAVA, supports both restrictive and elastic work of breathing in proportion to the patient’s inspiratory effort.

**Liquid ventilation**

Liquid ventilation is a technique of mechanical ventilation in which the lungs are insufflated with an oxygenated perfluorochemical liquid rather than an oxygen-containing gas.
Basics of Respiratory Support and Mechanical Ventilation

mixture. The use of perfluorochemicals, rather than nitrogen, as the inert carrier of oxygen and carbon dioxide offers a number of theoretical advantages for the treatment of acute lung injury, including:

- Reducing surface tension by maintaining a fluid interface with alveoli
- Opening of collapsed alveoli by hydraulic pressure with a lower risk of barotrauma
- Providing a reservoir in which oxygen and carbon dioxide can be exchanged with pulmonary capillary blood
- Functioning as a high-efficiency heat exchanger

Despite its theoretical advantages, efficacy studies have been disappointing and the optimal clinical use of LV has yet to be defined.

**Total liquid ventilation**

In total liquid ventilation (TLV), the entire lung is filled with an oxygenated PFC liquid, and a liquid tidal volume of PFC is actively pumped into and out of the lungs. A specialized apparatus is required to deliver and remove the relatively dense, viscous PFC tidal volumes, and to extracorporeally oxygenate and remove carbon dioxide from the liquid.

**Partial liquid ventilation**

In partial liquid ventilation (PLV), the lungs are slowly filled with a volume of PFC equivalent or close to the FRC during gas ventilation. The PFC within the lungs is oxygenated and carbon dioxide is removed by means of gas breaths cycling in the lungs by a conventional gas ventilator.

**NEGATIVE-PRESSURE VENTILATORS**

 Throughout the 19th century and the first half of the 20th century the negative-pressure ventilator was the predominant device used to provide ventilatory assistance. The first description of a negative-pressure ventilator was of a full-body type ventilator.
This “tank ventilator” was first described by the Scottish physician John Dalziel in 1838. It consisted of an air-tight box, with the patient maintained in the sitting position. Negative pressure was established by manually pumping air into and out of the box. The device was equipped with a pressure gauge to monitor the extent of negative pressure established in the device.

A number of other groups developed similar types of manually operated negative-pressure ventilators. In 1904 Sauerbrach even developed a negative-pressure operating chamber. The patient’s body, except for the head, was maintained inside the chamber. The chamber was large enough so that the surgeon was able to perform surgery while also in the chamber. The patient’s lower body was encased in a flexible sack so that positive pressure could be applied to this part of the body, preventing blood from accumulating in the abdomen and lower extremities, causing what was referred to as “tank shock.”

Negative-pressure ventilation became a much greater clinical reality with the development of the iron lung, originally designed and built by Drinker and Shaw, but manufactured and sold by Emerson. This approach to ventilatory support reached its pinnacle during the worldwide poliomyelitis epidemics from 1930 to 1960. The first ICUs were set up to manage in some cases dozens of patients, of all ages, requiring negative-pressure ventilation because of poliomyelitis. Boston Children’s Hospital developed a large negative-pressure chamber that could accommodate 4 children simultaneously and allow a nurse to care for the patients from inside the chamber.

Over time, numerous other types of negative-pressure chambers were developed and used, with varying success, such as the “raincoat” and the “chest cuirass”. However, in the 1960s there was a movement away from negative-pressure ventilation because of several factors. The first volume-targeted ICU/anesthesia ventilators began to appear. Second, the development of jet aviation at the close of the second world war lead to the development of small, compact, intermittent positive-pressure
breathing (IPPB) devices: the Bennett and Bird IPPB machines. Third, problems with the application of negative-pressure ventilation became too much for their continued use in the newly developing ICUs.

As a group, these devices were large, heavy, and cumbersome, and it was difficult to avoid excessive leaking (generally resulting in cooling of the patient’s body); they had a difficult time maintaining effective ventilation, were unable to sustain high airway pressure or establish PEEP, access to the patient was limited, and “tank shock” was an ongoing issue with full-body ventilators.

**POSITIVE-PRESSURE NONINVASIVE VENTILATION**

Positive-pressure noninvasive ventilation (NIV) can be traced back to biblical times: 2 specific passages from the Bible reference NIV: And the Lord God formed man of the dust of the ground and breathed into his nostrils the breath of life. (Genesis 2:7) And he [Elisha] went up, and lay upon the child, and put his mouth upon his mouth and the flesh of the child waxed warm.

However, the first mechanical apparatus used to provide NIV, a bag and mask manual ventilator, was introduced in 1780 by Chaussier. A more sophisticated bellows with a mask was introduced in 1887 by Fell, and in 1911 Dräger’s Pulmotor was first introduced. This was a fairly sophisticated pneumatically operated positive-pressure device that has been credited with saving thousands of individuals over its lifetime.

Another approach to providing NIV was introduced by Green and Janeway in 1910. They referred to their device as a “rhythmic inflation apparatus.” The patient’s head was placed into the apparatus and a seal was secured around the patient’s neck with positive pressure applied to the patient’s head. However, the most notable NIV devices of the 20th century were the Bennett TV and PR series and the Bird Mark series of ventilators. These devices were used primarily to provide intermittent treatments, as opposed to long-term ventilation, but in the 1960s and 1970s it was common
to see them used for life support in both noninvasive and invasive ventilation.

During the late 1970s and early 1980s, two things happened that changed the concept of NIV. First the IPPB machine faded from use as a result of reports that the use of the IPPB machine to deliver aerosolized medication was no better than a simple nebulizer and that incentive spirometer and blow bottle were as good as IPPB in preventing and reversing postoperative atelectasis. The second event was a series of case studies indicating that NIV could be used to provide ventilatory support to patients in an exacerbation of chronic lung or neuromuscular/neurologic disease, or to provide long-term ventilator support to those same patients.

In general, this type of support was first provided with volume control modes capable of only machine-triggered inspiration. But over time newer more sophisticated pressure-targeted ventilators designed specifically to provide NIV entered the market, and pressure-targeted ventilation became the norm for NIV. Today, NIV modes have become available on most new ventilators entering the market, and NIV has become the standard for initial ventilatory support for numerous pathophysiological conditions.

POSITIVE-PRESSURE INVASIVE VENTILATORS

First-Generation ICU Ventilators

Ventilators designed for positive-pressure invasive ventilation became available in the 1940s and 1950s. Some of the early models. The key distinguishing feature of these early invasive ventilators was that they provided only volume-control ventilation. Patient-triggered ventilation was not possible with these first-generation ICU ventilators. However, the range of sophistication of these ventilators was quite large. The Morch ventilator was a single-circuit, simple, piston ventilator. It was one of the least complex of this group and was designed to be placed under the patient’s bed. This ventilator had no monitors, no alarms, and no specific setting. The respiratory rate had to be counted and the tidal volume
measured with a secondary device. Gas was always delivered at an inspiratory/expiratory ratio of 1:2. On the other end of the spectrum was the Engstrom ventilator, which, because it had a double-circuit, could be used as an anesthesia machine or as an ICU ventilator. Although its monitoring capabilities were limited by today’s standards, it did include airway pressure and tidal volume monitoring and allowed for more exact setting of respiratory rate, but it still provided only machine-triggered inspiration at a 1:2 inspiratory/expiratory ratio. The Emerson postoperative ventilator was between those 2 extremes. It was also a volume-controlled ventilator and provided only machine-triggered inspiration, but it had an adjustable inspiratory/expiratory ratio and pressure and volume monitoring. But it could not be used for anesthetic gas delivery because it had only a single circuit.

This first generation of ICU ventilators did not incorporate PEEP. It was not until after the landmark paper by Ashbaugh et al that PEEP became a standard therapy in the ICU. With this generation of ventilators, PEEP was applied by placing the expiratory limb of the circuit under water, at a depth equal to the desired PEEP. This generation of ventilators ended in the early 1970s with the introduction of the Puritan Bennett MA-1 ventilator.

Second-Generation ICU Ventilators

The second generation of ICU ventilators differed from the first in a number of ways. Simple patient monitors were incorporated into the ventilator itself. Most monitored tidal volume and respiratory rate, but the most distinguishing feature of this generation of ventilators was patient-triggered inspiration. But still only volume ventilation was available. This also is the first group of ventilators that included basic alarms such as high pressure, high rate, and low tidal volume. Soon after the introduction of this generation of ventilators, intermittent mandatory ventilation (IMV) was introduced into adult ventilation. Downs et al published the first case series using IMV in 1973. They
used an external secondary IMV gas flow system introduced into the ventilator circuit. Later ventilators of this generation added demand values, and IMV became synchronized intermittent mandatory ventilation (SIMV). In addition to the MA-1, the Siemens Servo and Ohio 560 ventilators were typical ventilators of this generation. The introduction of the Servo 900C at the end of this generation introduced into clinical practice pressure-support and pressure-control ventilation.

In the late 1970s a publication by Hewlett et al provided a glimpse into the future of ventilator modes. They were the first to demonstrate the concept of closed-loop ventilation. Although their approach to mandatory minute ventilation was purely mechanical, it did function as a closed-loop controller and provided a model for many of the modes of today.

Gas entered this system at the left and preferentially entered a bellows from which the patient could breathe spontaneously. If the bellows filled completely, gas was directed to a second bellows. Once that bellows filled, gas from the bellows was delivered to the patient as a positive-pressure breath. Dependent on the flow of gas into the system, the setting of the bellows capacity, and the patient’s spontaneous minute volume, all breaths were either spontaneous or mandatory (if the patient became apneic) or a mix of the two. The primary problem with this initial system was that the patient could breathe the entire minute volume with a very rapid and shallow breathing pattern, but it did provide the first form of closed-loop control.

Third-Generation ICU Ventilators

Typical third-generation ICU ventilators were the Puritan Bennett 7200, the Bear 1000, the Servo 300, and the Hamilton Veolar. The single most important factor that all of these ventilators had in common was microprocessor control. This was a major event in the development of mechanical ventilators, because it meant that virtually any approach to gas delivery and monitoring was possible. All that was required was innovation, engineering
skill, and money! In addition, mechanisms for gas delivery were vastly enhanced. These ventilators were markedly more responsive to patient demand than any of the previous generations of mechanical ventilators.

Flow-triggering also became a reality, again reducing the effort patients needed to activate gas delivery. Almost every ventilator of this era included pressure support, pressure control, volume control, and SIMV. SIMV was not only available in volume ventilation, but also pressure ventilation and pressure support could be applied during the spontaneous breaths.

All of the ventilators of this generation also incorporated extensive alarms and monitors. They not only monitored the patient’s status, but almost every aspect of the ventilator’s functioning. This was also the generation of ventilators in which waveforms of pressure, flow, and volume were first introduced, along with pressure-volume and flow-volume loops.

With this generation of ventilators was the first use of airway pressure release ventilation, by Stock et al. The circuit used by Stock et al was a simple high-flow system that incorporated a solenoid valve and 2 PEEP valves. The approach applied high levels of continuous positive airway pressure (CPAP) but periodically reduced the CPAP to a lower level to assist with ventilation. The solenoid could be programmed to apply any ratio of inspiratory and expiratory time between high and low CPAP, as well as any frequency of dropping to the low CPAP level.

**Fourth-Generation ICU Ventilators**

This is the current generation of ICU ventilators, which are the most complex and versatile of any mechanical ventilators ever manufactured. In this era there has clearly been a marked increase in the number of ventilators, of all possible types. Numerous ventilators classified as ICU ventilator are available worldwide. There are a number of what have been referred to as sub-acute ventilators, as well as transport/home-care ventilators and ventilators designed specifically for NIV applications.
The single feature that distinguishes this generation is the plethora of ventilation modes available. In addition, many of these new modes are based on closed-loop control. The question that we all should be asking manufacturers regarding these new modes is, “Do they provide value, or are they simply more bells and whistles?” The questions I use to determine if a new ventilation mode is useful are:

- Does it make ventilation safer?
- Does it decrease the likelihood of ventilator-induced lung injury or hemodynamic compromise?
- Does it more effectively ventilate or oxygenate the patient?
- Does it wean the patient from ventilatory support faster?
- Does it improve patient-ventilator synchrony?

If the answer to each of those questions is no, then the mode is essentially useless. Fortunately, most of these newer modes do seem to have a yes answer to at least one of the questions.

Most of these new modes are, for the most part, based on a pressure-targeted approach. Maybe the most complex of these modes is adaptive support ventilation, which attempts to establish a ventilatory pattern based on the Otis work-of-breathing model. The clinician enters the patient’s ideal body weight, desired minute volume, and maximum airway pressure, and the ventilator determines the respiratory rate and tidal volume combination that results in the least work of breathing. This pattern is established by the ventilator automatically adjusting the ventilating pressure and respiratory rate. In the newest version of this mode, end-tidal $P_{CO_2}$ is also added as an input. Initial data suggest that this mode works well in some patients. But, like all of these modes, additional research is needed to identify when it should be used.

SmartCare is another form of closed-loop control of pressure support for weaning. The ventilator automatically adjusts the pressure support level every 2–4 min to maintain a predefined respiratory rate, tidal volume, and end-tidal $P_{CO_2}$, with separate algorithms for COPD patients, for use with endotracheal tubes.
versus tracheostomy tubes, and for those with active versus passive humidification. When the pressure support level is reduced to a predetermined level, the ventilator automatically performs a spontaneous breathing trial (SBT). If the patient fails the SBT, the ventilator automatically resumes ventilation.

If the patient passes the SBT, the ventilator notifies the user that the patient should be considered for extubation. A recent randomized controlled trial compared SmartCare to clinician-performed weaning and found that patients were weaned faster with SmartCare. The study has been criticized because in the control arm the clinician-applied SBTs were not consistently performed, being missed 50% of the time. A more recent study in which the control group was weaned per the protocol, found no benefit from SmartCare. However, in the real world, modes of this type are very useful, because they ensure that when the patient meets defined criteria, the appropriate care is provided regardless of how busy the clinician may be.

Proportional assist ventilation and neurally adjusted ventilatory assist are available on the fourth generation of ventilators, but should be considered modes of the future. With both of these modes, pressure, flow, volume, and time are not set. What is set is the proportion of a patient’s ventilatory effort that is unloaded without forcing a ventilatory pattern. Proportional assist ventilation functions by responding to the mechanical output of the diaphragm and accessory muscles of inspiration (inspiratory flow and volume), whereas neurally adjusted ventilatory assist functions by responding to the neural input to the diaphragm (electrical activity). Data from physiologic studies of these modes indicate that, when patients are transitioned to either mode, synchrony improves, tidal volume decreases, respiratory rate increases, and peak airway pressure decreases, without adverse effects on gas exchange or hemodynamics. No randomized trials comparing these modes to conventional mechanical ventilation have been published to date, but we expect that the ability of these modes to improve patient outcomes will be shown in the future.
Almost all of the ventilators in this generation include NIV modes, and many are capable of ventilating neonates as well as adults. Currently the capability of the NIV modes on these ventilators varies widely. Some do a good job of compensating for leaks, whereas others do not. However, we predict that all of these ventilators will eventually provide NIV with the same efficacy as the ventilators designed specifically to provide NIV. As shown by Marchese et al, most of these ventilators are at least as capable of meeting the demands of neonates as a traditional neonatal ventilator. I expect that their function at this level will improve over time.

All of the ventilators of this generation are easily upgradable, include waveforms as a basic operating feature, and provide extensive monitoring. Each of them provides monitoring data of 20 to 40 individual variables. Many provide multiple screens of data presentation. Almost every possible patient and ventilator variable is displayed. Trending data are also available on most of these units.

Some of these ventilators include specific management/assessment packages. Some allow the clinician to program the performance of a pressure-volume loop. Others have programs that make it easy to perform recruitment maneuvers or decremental PEEP trials. Others have options that facilitate assessment for weaning and performance of weaning trials, whereas others allow for measurement of esophageal pressure and functional residual capacity. The current generation of ICU ventilators is far ahead of the ICU ventilators we used in the 1960s or 1970s. Considering how much change has occurred in ICU ventilators over the last 50 years, one can speculate on the future of ICU ventilators.

**THE FUTURE ICU VENTILATOR**

The ICU ventilator of the future may not look very different from today, but several features will clearly separate them from the current generation of ventilators. There will be integration
with other bedside technology. Within a few years, all ICUs will have electronic charting, where data from all bedside technology will be transmitted to electronic documentation systems. As a result, ventilators must be able to be integrated electronically with all other bedside technology.

The days of specific ventilators designed to do specific tasks such as neonatal ventilation, adult ventilation, NIV, and transport will be gone. The ICU ventilator of tomorrow will be able to perform all of these tasks as well or better than the individual ventilators of the past. The available evidence indicates that some ventilators are already capable of providing ventilation under multiple situations, and in the future all will.

Protocols will become part of the basic operation of the ICU ventilator. As more evidence becomes available on how we should provide lung-protective ventilation, and on how we should manage specific diseases, ventilators will be able to integrate evidence-based algorithms into their basic operational approach. We should be setting tidal volume based on the patient’s predicted body weight.

The ventilator of the future will require us to input the patient’s height and sex, and volumes will be presented as mL/kg predicted body weight, in addition to absolute volume. The Acute Respiratory Distress Syndrome Network protocol, as well as different approaches to performing lung-recruitment maneuvers and setting PEEP, will be selectable options on future ventilators. These approaches will still require the clinician to set basic parameters, but the ventilator will provide guidance to assure that ventilation for a specific disease state is performed within the current best evidence-based guidelines.

Much of the noise pollution in the ICU is a result of alarms. However, in the vast majority of circumstances the alarms are false. As a result, staff are programmed to ignore alarms ("alarm fatigue"). The ventilator of the future will correct this. Smart alarms will replace our current systems. For example, the high-
pressure alarm does not need to sound every time pressure exceeds the set level. The ventilator of tomorrow will be able to identify the pattern of alarms.

We would interpret the following 3 scenarios differently, and there is no reason why the ventilator could not do the same thing. First, a periodic increase in airway pressure that exceeds the set level on an occasional basis. Second, a slowly increasing peak pressure over a number of hours with the tidal volume unchanged. Third, airway pressure increasing with each breath and the delivered tidal volume, once the limit is met, getting smaller with each breath. All 3 of these scenarios represent potential clinical situations with different levels of urgency in their response.

The first is most likely a result of secretions in the patient’s airway or water in the ventilator circuit that periodically causes the peak airway pressure to rise. This is not an emergency. The second situation depicts a change in the patient’s lung mechanics, requiring the clinician to determine the cause and potentially to adjust the ventilation approach. But this is not an emergency. The third scenario, however, is an emergency. This potentially indicates that a tension pneumothorax has developed and requires immediate response. Clearly the alarm conditions in these 3 scenarios should be markedly different. The ventilator of tomorrow will be able to interpret these patterns and the alarm conditions will be different.

The ventilators of tomorrow will not present lists and lists of unrelated data that are of little use to the clinician. An individual can process only finite individual pieces of data. The next generation of ventilators will present information: not merely lines of data. Easy to interpret graphs or figures will be displayed that allow the clinician to rapidly determine if the patient’s status has changed. The use of a figure to represent a change in patient’s status is already being used on at least one ventilator. Important interrelated variables will be presented so the clinician can rapidly determine if change has occurred. For example, tidal volume and airway pressure will be presented in a manner that the trends in these
variables can be easily understood. In addition, information that traditionally has not been presented will be provided. The asynchrony index will be calculated and displayed, along with the number of breaths with missed triggers, with double-triggers, or that have an exceptionally short or long inspiratory or expiratory time. The presence of conditions that are associated with the development of auto-PEEP will be identified and displayed.

The most important thing that this new generation of ventilators will do is provide decision support. Each alarm condition will be followed with a listing of potential causes and potential solutions. Changes in ventilator variables will be identified and the clinician notified of the change, the potential causes, and the possible solutions. A library of information will be accessible from the ventilator screen, ranging from the ventilator’s operation manual to the evidence that supports a recommended action.

Closed-loop control of ventilation will be available on all ventilation modes. These new ventilators will be able to adjust gas delivery to improve patient-ventilator synchrony. They will be able to interpret the airway pressure and flow waveform during both volume and pressure ventilation, and to automatically adjust the flow waveform, peak inspiratory flow, rise time, and termination criteria to ensure that gas delivery is synchronous with the patient’s desires. This is an increasingly important factor in ventilator functioning, because we are finding out that patient outcome may be markedly affected by asynchrony. Automatic adjustment of termination criteria is already available on at least one ventilator.

All of these expected changes mean that the users of the mechanical ventilators of the future will have to be even better prepared than the users of today. They will have to understand in detail the operational complexities of the new features. They will have to be able to determine when one feature is indicated over the other. They will have to make sure that the ventilator is truly doing what it is expected to do and that the patient is responding as expected to the intervention. The clinicians managing
these patient-ventilator systems of the future will need to be much more capable than the current group of operators.

The historical development of the mechanical ventilator is truly a remarkable journey. In just 50 short years we have gone from relatively crude, totally mechanical devices that could provide only machine-triggered volume ventilation to highly evolved microprocessor controlled systems capable of any form of ventilatory support imaginable. The evolution of the mechanical ventilator mirrors the evolution of the profession of respiratory care as well as critical care medicine, and may even be the primary reason that respiratory care has grown to its current status. Finally, the single most descriptive term that will be used to define the future generation of mechanical ventilators will be smart.
Neonatal Intubation (Specific Considerations)

BASIC ANATOMY AND PHYSIOLOGY OF THE NEONATE

The cricoid cartilage is the narrowest portion of the larynx in a neonate. A 3.5 mm size internal diameter endotracheal tube (ETT) is usually appropriate for full-term neonates and 2.5-3 mm is used for smaller or premature infants. The commonly used blades for laryngoscope in neonates are Miller size 0, 1 and Wis-Hipple blades and 000 face mask and 0-sized laryngeal mask airways should be available. Infants operate close to closing volume during tidal breathing resulting in more rapid anaesthetic gas uptake as well as more rapid desaturation during apnoea. Volume replacement and maintenance of heart rate are essential for maintenance of blood pressure in new borns. Immaturity of the blood and blood vessels increase the risk of intra-ventricular haemorrhage (IVH) in the neonatal period. The first 72 h of neonatal life is the risk for IVH. Hypoxia, hypercarbia, fluctuations in blood pressure or venous pressure, high or low haemoglobin and pain increase the risk of IVH.

Pharmacology

Immature tubular function in neonate results in decrease
clearance of some drugs, especially morphine and immature liver function also results in decreased biotransformation of many drugs (eg, opioid/local anaesthetics). All drug doses are to be calculated before commencing anaesthesia.

The immaturity of blood brain–barrier results in higher cerebrospinal fluid opioid level in the newborns. Remifentanil, an ultra-short-acting opioid is useful for its volatile sparing effect and for neonates at risk for post-operative apnoea who are to be extubated after completion of surgery. Newborns require higher dose of succinylcholine (2 mg/kg).

Mivacurium and cisatracurium possess a more predictable duration of action, provided the infant is normothermic and devoid of significant cardiovascular side effects. The duration of action is shorter in neonates. Rocuronium and vecuronium have prolonged duration of action in neonates. The use of bupivacaine, for caudal epidural anaesthesia is associated with higher blood level in neonates.

The level may continue to rise for more than 48 h from the time of administration. There is a risk of using lidocaine due to its toxicity, but it can be used safely because the blood level of lidocaine can be easily measured. Chlorprocaine can be used with greater safety in the newborns. Sevoflurane has less effect on infant hemodynamics compared with halothane and may be preferred to halothane.

Time of emergence is significantly faster with desflurane and beneficial in neonates in whom extubation is planned. Nitrous oxide is contraindicated in many neonatal surgical emergencies. Thiopentone (5-6 mg/kg) is being used as induction agent in neonates. Propofol causes moderate-to-severe hypotension and hypoxia when used in a dose 2-3 mg/kg. Ketamine is a very useful induction drug for patients with compromised hemodynamic critically ill patients. Fentanyl has minimal cardiovascular depressant effects so it is used in critically ill patients, 12 ìg/kg for abdominal surgery, and 50 ìg/kg for thoracic surgery.
Remifentanil is a very-short-acting drug and useful where extubation is desirable at the end of surgery. Dexmedetomidine is useful if one wishes to keep a patient sedated and spontaneously breathing to do awake intubation; however, decrease in heart rate and blood pressure do occur sometimes.

Pre-operative evaluation

A detailed history and physical examination is very important. The history includes gestational age, significant events at birth (asphyxia, meconium aspiration, Apgar score) and ventilatory support. The physical examination includes hydration status and co-existing diseases. Laboratory examinations include a recent haematocrit, glucose and calcium. Neonates are at risk for hypoglycaemia and dehydration. Six hours for formula milk, 4 h for breast milk and 2 h for clear fluid are appropriate fasting for most neonates. A discussion with parents includes the planned conduct of anaesthesia, pain relief, post-operative monitoring, blood transfusion, invasive monitoring, admission to HDU and paediatric intensive care unit (ICU).

Intra-operative management

Neonates are extremely susceptible to hypothermia. The consequences of hypothermia include pulmonary hypertension, delayed drug metabolism, hypoxia and apnoea. Care is taken during transport and intra-operative period. They are to be provided a neutral thermal environment (warm operating room) and transport them in a heated module. Warm humidified inspired gases, warm antiseptic solution and for intra-operative irrigation, warm blood and intravenous (IV) fluid, heated mattress, radiant warmer, Bair–Hugger warmers are ideal for them. Heated hot air circulation under the drapes and microprocessor controlled device (Allon system), which heats/cools the re-circulating water contained in a garment covering the patient have been found to be effective in maintaining perioperative normothermia. Optimal monitoring includes precordial stethoscope, pulse oxymeter, capnograph, noninvasive blood pressure, electrocardiogram (ECG)
and thermal probe (oesophageal/rectal). Monitoring of urine output (5Fr feeding tube) as urinary catheter is advised for major surgery. Intra-arterial catheter (IAC) is useful in critically ill neonates. Central venous pressure catheter (3Fr) is placed usually in the right internal jugular vein, useful for monitoring and IV access. Commonly 24G and 22G are the largest IV catheters that can be inserted peripherally.

Additional monitoring may be inspired airway pressure and neuromuscular function. Fluid considerations for neonates follow similar lines to those of adult patients. For neonates, the maintenance fluid consists of hypotonic glucose solution (dextrose 5 or dextrose 10 with water or 0.2 normal saline) and for replacement of insensible (third space) and small volume blood loss, isotonic fluid may be administered separately.

To prevent excessive fluid (and glucose) administration it is wise to run both maintenance fluid (4 mL/kg/h) and operative (insensible and blood loss) fluid replacement (3-10 mL/kg/h) on infusion pumps. During neonatal surgery glucose administration can be continued but blood glucose measurement is essential. Hypoglycaemia is defined as blood glucose level below 45 mg/dL, first 3 days of life and 75 mg/dL thereafter.

Response to fluid therapy is monitored by variations in heart rate, blood pressure and central venous pressure. In the neonate epidural analgesia may be indicated when the goal is early extubation (after tracheo-oesophageal fistula) or spontaneous ventilation (eg, following congenital diaphragmatic hernia (CDH)) to avoid barotraumas. These goals are relevant in developing countries where facilities are limited or stretched.

Caudal anaesthesia has become the most valuable adjunct to general anaesthesia. Epidural catheters provide optimal analgesia when the tip of the catheter is placed at centre of dermatomes affected by surgery. Safe blood levels of bupivacaine have been found after bolus injection of 1.5-2.0 mg/kg bupivacaine (0.6-0.8 mL/kg of 0.25% bupivacaine) followed by a continuous infusion.
of 0.2 mg/kg/h. Lidocaine (1 mg/kg) may prove safer. Chlorprocaine (10-15 mg/kg) may be used with less risk of toxicity. With ultrasound-guided nerve block, careful monitoring, regular audit, the safety of regional anaesthesia in neonate will continue to improve.

**Post-operative considerations**

Some procedures require a period of post-operative ventilation, but in many cases return to neonatal unit or high dependency unit is anticipated. Immediate post-operative extubation in the neonate require that the patient is awake with full strength (hip flexion, arm lifting), have a low likelihood of airway obstruction (normal airway anatomy), normal temperature, blood pressure and volume status and regular respiratory pattern with adequate minute ventilation. Risk of post-anaesthetic apnoea (PAA) is considered in all patients born prematurely (less than 37 weeks of gestation), regardless of anaesthetic technique. The factors which increase the risk for PAA are hypothermia, hypoglycaemia, hypoxia, sepsis and hypocalcemia, which occurs with greater frequency in neonates who undergo emergency surgery. Use of apnoeic mattress or transthoracic impedance monitoring through the ECG leads is commonly used. Oxygen saturation monitor, heart rate, blood pressure, temperature, blood glucose, central venous pressure, urine output, observation of stoma or wound drainage is inevitable. Post-operative fluid management varies with surgical procedure and general condition of the neonate. Electrolytes are checked daily. Total parenteral nutrition may be required in some patients.

In abdominal surgery having no feeding since birth, most newborn abdominal surgical emergencies are considered “full stomach” and they require volume loading (10-20 mL/kg Ringer’s lactate solution) and pre-oxygenation (1 min) before induction.

**Tracheo-oesophageal fistula/oesophageal atresia**

Tracheo-oesophageal fistula/oesophageal atresia (TEF/EA) is a relatively common congenital malformation occurring in 1:3000-
4500 live births. Commonly TEF is of 5 types (A-E), with type C being the most common. It is commonly diagnosed in the delivery room when suction catheter cannot pass from mouth to stomach.

Infants with TEF are premature (20-30%) and they have a high incidence of congenital heart disease and other anomalies. In all infants of TEF, echocardiography and chest X-ray are ideally done. The aortic arch side can be identified as the surgical incision will be made on the opposite side.

Until the workup is completed surgery may be delayed. Infants have pooling of secretions in the pouch so they have to be kept in a semi-upright position with a drainage catheter on low suction in the pouch. Before induction, atropine 20 ìg/kg can be given to neonates. The pouch has to be aspirated and inhalational induction can be performed with avoidance of positive pressure ventilation to prevent gastric distention.

The infant is intubated deep without muscle relaxant and gentle positive pressure ventilation (PPV), the location of fistula is identified by listening over the lungs and stomach. In premature infants, an awake intubation is preferred. Induction with sevoflurane or halothane allows spontaneous respiration, and adequate anaesthetic depth may be associated with hypotension, hypoventilation and coughing.

The tube is tapped at a location below the fistula but above the carina. If the fistula is at the carina the tube may be advanced into the bronchus of the lungs on the non-operative side. There are a number of proposed methods of estimating the correct ETT position: Manipulating the ETT during auscultation; placing the tracheal tube into the bronchus and withdrawing until air entry is heard bilaterally; and rotating the ETT so the bevel faces anteriorly away from the fistula. A cuffed ETT may also provide assistance in occluding the fistula. Many surgeons do a rigid bronchoscopy after induction to locate the fistula. Occlusion of the fistula with a Fogarty catheter, either with the bronchoscopy or less commonly in a retrograde
manner via a gastrotomy may be done to isolate the airway from the gastrointestinal tract.

Care to be taken to avoid tension pneumothorax during bronchoscopy by limiting insufflations of oxygen via the bronchoscope. When the patient is settled and positioned for right thoracotomy or neck incision, the job of anaesthesiologist is to guide the surgeon to locate the proximal oesophageal pouch and fistula. For that a red rubber catheter or infant feeding tube is placed in proximal pouch.

Tube is pushed time to time to make proximal pouch prominent on demand of surgeon. When thoracotomy is done the lung is packed away to mobilise the distal segment of oesophagus for anastomosis, which may lead to oxygen desaturation. Anaesthesia for bronchoscopy, intubation and TEF repair can be induced by IV agents, inhalational agents or combination of both the techniques with additional use of local anaesthetics and opioids.

A recent study of Atzori et al. concluded that tracheobronchoscopy is a useful and safe procedure and to be recommended in tertiary centres for infants with oesophageal atresia before surgical repair. Knottenbelt et al. in their study concluded that the usefulness of routine bronchoscopy and best management of a large TEF need to be defined.

If ventilation can be accomplished without gastric inflation; the patient can receive muscle relaxant. Usually gentle bagging will ventilate the lungs. Bleeding into trachea during surgical manipulations can cause blockage of ETT. So suction or replacement of the tube is needed if blockage cannot be cleared. Airway pressure is kept to a minimum during the entire procedure.

IV fluid is used with caution. An umbilical arterial line may be a good alternative to radial and femoral line. IAC is advisable for arterial blood gas and patients with unstable haemodynamics. Fentanyl may be used intra-operatively and as continuous infusion for post-operative analgesia. Paracetamol can also be given rectally or IV for post-operative analgesia. A caudal catheter can be
advanced to T₆-T₇ to supplement the general anaesthesia (isoflurane/sevoflurane/desflurane/air/oxygen) and provide excellent post-operative analgesia without use of opioid and to facilitate extubation. New catheters (Flex Tip plus™) have incorporated a coiled wire to improve ultrasound visualisation.

Local anaesthetic clearance is reduced in neonates. Maximum dose of local anaesthetic is to be reduced and the duration of infusion should be maximum up to 48 h post-operatively. Local infiltration, intercostal block, paravertebral blockade or intrapleural infusion of local anaesthetics can be considered.

Most infants are extubated if they are awake. Infants smaller than 2000 g may require post-operative mechanical ventilation. There is a debate whether risk of reintubation is greater in these infants than the risk of continued intubation with respect to the site of fistula.

Dynamic collapse of the trachea during inspiration can occur presenting with increase in child’s respiratory effort. Tracheopexy may be necessary or a tracheotomy may be required. In a recent study conducted by Al-Mendalawi et al., mortality rate due to TEF is maximum due to respiratory failure and rest are due to sepsis and cardiac arrest during anaesthesia is the least. Endoscopic surgical procedures for TEF are becoming an attractive alternative to open procedures. Use of Proseal laryngeal mask airway which allows drainage of gastric fluid and air, can decrease the chances of unwanted gastric insufflations.

Omphalocele/Gastroschisis

Both omphalocele and gastroschisis look similar but are different due to defects of abdominal wall. The incidence of omphalocele is 1:6000 live births, whereas the incidence of gastroschisis is 1:15000 live births. In omphalocele there is a mid-line defect and is associated with other anomalies, whereas gastroschisis is not. In both the cases large fluid resuscitation is required before, during and after surgery. In a study conducted by Chirdan et al. in African countries, where silos are not available,
an infusion bag may be used for temporary cover of eviscerated bowel. So reported mortality and morbidity from ruptured exomphalos and gastroschisis from Africa is quite high.

These patients are considered as full stomach. Anaesthetic maintenance can include fentanyl in addition to inhalational agent as the increased intra-abdominal pressure and diaphragmatic elevation reduces respiratory compliance and makes extubation inadvisable. Nitrous oxide should be avoided. Maintenance of body temperature is essential. Continuous epidural injection provides analgesia, motor blockade without respiratory depression and may reduce the post-operative ventilation. Isotonic fluid (10 mL/kg/h or more), colloid (albumin), sometimes dopamine infusion may be necessary. Warm irrigation fluid is administered.

**Pyloric stenosis**

The incidence of pyloric stenosis (PS) is 3:1000 live births. Symptoms are apparent from 2\textsuperscript{nd} to 6\textsuperscript{th} week of life. Neonates have severe projectile non-bilious vomiting with resultant hypochloraeic dehydration. Before surgery, measurement of electrolyte and correction of hypovolaemia and alkalosis can be done by administration of 10-20 mL/kg of isotonic fluid. The goal is to lower the serum HCO$_3^-$ to less than 30 mEq/L. Maintenance fluid of D5, 0.45 NS at 4 mL/kg/h can be administered. Although alkalosis is usually associated with hypokalaemia, 36% of cases with PS present with hyperkalaemia. Orogastric tube is placed and suctioned after 0.15 mg/kg atropine administration, with the infant turned side to side to empty the stomach prior to rapid sequence intubation and cricoid pressure with placement of 3.5 mm ETT or the size, which yields a leak of 10-25 cm H$_2$O. Nitrous oxide is avoided. Maintenance of anaesthesia is by inhalational agent with remifentanil. Local infiltration technique can be used for the operation also. Post-operatively wound infiltration, rectal acetaminophen and ketorolac are very useful. Awake intubation is safer. Blood glucose monitoring is essential. Oral feed may be started 4-6 h of surgery in some cases.
Necrotising enterocolitis/intestinal obstruction

Necrotising enterocolitis (NEC) is primarily seen in premature [preterm (less than 32 weeks) and low birth weight (less than 2 kg)] infants, whereas intestinal obstruction manifests in 2nd to 6th week of life with incidence 1:2000. NEC occurs as a result of bowel ischemia and hypotension due to poor cardiac output state, infection, and others, whereas intestinal obstruction is due to congenital malformations, such as duodenal/jejuna atresia, Ladd band, rotations and others.

These emergencies share the same clinical picture with abdominal distention, hypotension, coagulopathy, sepsis, dehydration and electrolyte imbalances. These neonates are critically ill and usually come to operation room with ETT and inotropes. Judicious fluid management is required for NEC (70 mL/kg) and intestinal obstruction (20 mL/kg isotonic crystalloid) to combat the dehydration.

Rapid sequence induction with cricoid pressure is preferred. In debilitated patients awake intubation can be done. Naso-gastric tube is essential for gastric decompression and remained on suction during induction and intubation to minimize the amount of gastric contents on oropharynx.

Ketamine 4 mg/kg/h combined with fentanyl 10-30 ìg/kg and a muscle relaxant can be administered. Inhalational agent can be used with caution nitrous oxide is contraindicated. Blood, Fresh Frozen Plasma, platelet, dopamine, adrenaline in low dose may be necessary. Light general anaesthesia and epidural analgesia are contraindicated due to sepsis and coagulopathy in NEC. However, this may be considered in intestinal obstruction to avoid need for post-operative ventilation. IAC is advisable as hypotension and frequent laboratory assessment may be necessary. Post-operative management may require meticulous fluid management, inotropic and ventilator support and antibiotics. Sometimes neonates are managed with placement of an abdominal drain percutaneously in the neonatal ICU with IV analgesia/sedation.
Congenital diaphragmatic hernia

The incidence of congenital diaphragmatic hernia (CDH) is 1:2500 live births. Herniation of abdominal viscera into thoracic cavity leads to pulmonary hypoplasia due to compression by the viscera on developing lungs. To improve ventilation high-frequency ventilation, Extra Corporeal Membrane Oxygenator, nitric oxide and pulmonary vasodilators are used but nitric oxide use is controversial. Chirdan et al. concluded in their study that in African countries most of the severe cases of CDH are missed and the infants die in the immediate post-natal period. Other factors predicting poor prognosis are PaO$_2$ less than 80 mmHg or PaCO$_2$ more than 40 mmHg after therapy. Before coming to operation room (OR), the patient has to be stabilised. This may take 10 days in severe pulmonary hypertension. In the OR high volumes or ventilation pressure has to be used carefully as there will be trauma to healthy lung. Listening to breath sounds beforehand and knowing the hernia is on left or right side are important. An oro-/naso-gastric tube is inserted. Neonates who are not intubated before arrival in the OR are generally intubated awake or after rapid sequence induction. Analgesia may be administered. High inflation pressures for mask ventilation are avoided. Pentothal and fentanyl can be used. IAC is recommended. Hypoxia, acidosis and hypothermia are avoided. Blood loss is to be taken care. Sometimes hernia is repaired while a child is on extra corporeal membrane oxygenator (ECMO) despite hemodynamic and pulmonary instability. Isoflourane can be used by administering it through ECMO circuit. Drug also can be given directly to patient or ECMO circuit. Patient on ECMO are heparinised. Intra-operative bleeding can be problematic because haemostasis is abnormal.

CONSIDERATIONS FOR INFANTS AND SMALL CHILDREN

Pediatric considerations are difficult because of the varying physical sizes of children. Adolescents may be as large as adults. Certain aspects (such as measurements and equipment) may be
the same as adults, while other dimensions (such as psychology, continued growth, drug concerns, and cultural/legal issues) are more similar to children. The team must use good judgment.

The ABCs are still the most important aspect of any resuscitation, but special aspects of the physiology and anatomy of children need to be recognized. This is not intended to alarm the emergency care team but rather to assuage the natural tendency to be anxious about the responsibility of resuscitating small children. Do not withhold aggressive resuscitation because of fear of the unknown.

**Children are not small adults.**

The child’s caregiver adds another complex dimension to resuscitation of children. Patients are often scared and incapable of (much) interaction or cooperation. Assume that anxiety will complicate the evaluation. Deal with anxiety proactively and appropriately. Explanations and honest reassurance help to relieve anxiety and to gain the support of the caregiver.

The decision for family and/or caregivers to be present during resuscitation efforts is a delicate one, considering both the emotional needs of the family and the healthcare providers’ need to focus on the patient. Most families want to be in the room during resuscitation efforts. But their presence may also transform a focused, technical environment into a highly emotional one. Remember, the health care providers’ first responsibility is to the patient. Many elements need to be in place in order that family presence during resuscitation does not jeopardize patient care. These include: Available staff to stay with family to explain and continually assess the family members’ ability to withstand the situational trauma, a controlled environment relatively free of chaos, continued assessment of the appropriateness of family members’ presence, and a willingness to remove family members should the situation require.

Another serious impediment to effective and expedient resuscitation of small children is the need for specific information
about drug dosage and equipment sizes. Keep manuals and tables that provide rapid answers to such questions available. The Broselow Pediatric Emergency Tape is a handy reference in the emergency facility. (Vol I—ACUTE CARE PORTALS Pediatric Equipment Sizes)

Pediatric variations include:

1. An infant is unable to maintain body temperature without support because of a large surface area (relative to body mass) and also because the autonomic nervous system is immature at birth. An infant is unable to shiver. An infant is unable to shunt blood away from the skin when he or she is cold. Keep infant dry and warm.

2. Infants < 6 months of age are nose breathers. Secretions and foreign bodies easily obstruct their small upper airways. The larynx and trachea are also small and easily occluded. While asleep or unconscious, make sure infant’s airway is open.

3. The cartilages of an infant’s larynx and trachea are soft and easily compressed by hyperextension and hyperflexion of the neck, resulting in airway obstruction.

4. An infant’s trachea is surprisingly short. The length of the trachea is not proportional to that of an adult. Remember size so as not to intubate the right main stem bronchus.

5. The cricoid cartilage forms the narrowest part of the airway in infants and small children. An ET tube that can be inserted past the vocal cords might still be too large to get past the cricoid cartilage. The cricoid cartilage forms an effective seal around the ET tube in children < about 6 to 8 years of age. However, cuffed tubes are now preferred because they prevent air leaks, making ventilation easier.

6. An infant’s upper airway is very reactive, at times making ET intubation difficult. Stimulation of the hypopharynx may cause a vigorous gagging motion and laryngeal spasm. Because infants are sensitive to vagal stimulation atropine is used in RSI.
7. The intercostal muscles are poorly developed in infancy, the result being that an infant relies heavily on diaphragmatic movement to breathe. For this reason, gastric and abdominal distension in infants can severely interfere with respirations. Another effect is the inability of infants to sustain increased effort when the work of breathing (WOB) is increased for any reason. When bagging an infant, perform Sellick’s maneuver to prevent air from blowing up the infant’s stomach. Insert a nasogastric tube as soon as possible after intubation.

8. The sternum and ribs of a small child are soft and compliant. They are not easily broken, but the viscera of the chest are at risk for compression injury, even without rib fractures. The compliant chest wall also retracts easily when there is airway obstruction. In small children with upper and lower airway obstruction, rib and supraclavicular retractions are early signs. This apparent increase in the WOB is useful for indicating distress.

9. In children < 1 year of age, barotrauma is easily produced in the lungs by positive pressure ventilation (PPV). Tidal volume is small, and the respiratory rate is fast, the result being that well-meaning team members may easily hyperinflate the lungs using mechanical devices or mouth-to-mouth breathing, which results in pneumothorax.

10. Pneumothorax in infants is especially likely to result in tension pneumothorax because the mediastinum may shift easily with resulting decreased filling of the heart and compression of the opposite lung.

11. The cardiac chambers of infants and small children are small. The myocardium itself is relatively stiff. There is little room for stroke volume reserve. Small children respond to a need for increased cardiac output by beating their hearts faster. With bradycardia or a heart rate > about 200 bpm, cardiac output falls dramatically.
12. Daily water exchange is great. Dehydration occurs quickly and to a high degree with increased fluid loss or decreased fluid intake.

13. The blood volume of young children is small in absolute terms, but their cardiac output is high relative to adults. This results in a small circulating blood volume reserve. On the other hand, small children have a highly reactive vascular tree that can mask relatively large volume losses. When small children finally decompensate, they are in mortal danger.

14. In small children, urine output alone might not be a sensitive indicator of the adequacy of perfusion because renal immaturity may prevent the renal shutdown commonly seen in adults. When renal shutdown does appear, it is a late finding.

15. CNS and autonomic nervous system immaturity may mask seizure activity in infants and small children. Any repetitive muscle motion, including eye and diaphragmatic motion, may represent seizure activity.

16. BP, pulse, and respiratory rate vary substantially from that seen in adults. Infants have a systolic BP of 70 to 80 torr, a pulse rate of up to 160 bpm, and a respiratory rate of 25 to 50/min.

   Toddlers have a systolic BP or 80 to 90 torr, a pulse rate of up to 140 bpm, and a respiratory rate of 20 to 35.

   Older, pre-pubertal children have a systolic BP of 85 to 95 torr, a pulse rate of 60 to 100, and a respiratory rate of 18 to 30.

   To estimate normal systolic BP, a good rule of thumb is to multiply the child’s age in years by 2 and add 70.

17. To estimate body weight: In children > 1 year, multiply the child’s age in years by 2 and add 10 to equal weight in kg. In children < 1 year, multiply the child’s age in months by 0.5 and add 3.5 to equal weight in kg. (This does not work for overweight children.)
18. The anterior fontanelle closes at about 18 months of age. Until then, it provides a means of assessment for ICP. Palpation of the open fontanelle can detect both dehydration (indicated by depression of the fontanelle) or increased ICP (indicated by bulging), as in meningitis or cerebral edema.

19. Vasovagal reflexes are prominent in small children. Intubation, pharyngeal stimulation, and medications (such as succinylcholine and ketamine) may cause marked bradycardia. Prior to these measures (and whenever feasible), use atropine at 0.02 mg/kg with a minimum dose of 0.1 mg and a maximum single dose of 0.5 mg.

20. In almost every emergency situation, consider the possibility of child abuse. Examination of the retina may reveal hemorrhage resulting from the child being shaken. Clues include unusual bruising, unexplained fractures, burns, and an unusual reaction to strangers and caregivers.

21. Remember, *all that wheezes is not asthma*. Also consider foreign bodies, bronchiolitis, pneumonia, other causes of thick secretions, and acute respiratory distress syndrome (ARDS).

22. Rapid sequence intubation (RSI) requires IV access and is therefore dependent on the cooperation of the patient. Repeated IV attempts may upset a child with a compromised upper airway and cause consequential struggling, secretions, and anxiety as well as a decreased probability of securing the airway. An alternative to proceeding directly to IV access is to sedate children by using the following regimen: ketamine 3 to 4 mg/kg IM, atropine 0.02 mg/kg (0.1 mg minimum) IM, with or without midazolam 0.1 mg/kg IM. Then, pursue IV or IO access and further paralysis as needed. Do not sedate the respiratory patient unless you plan to secure the airway. Sedation allows definitive airway control.
Neonatal Intubation (Specific Considerations)

PHYSIOLOGIC RESPONSES TO INTUBATION

The process of intubation may cause hypoxemia, bradycardia, intracranial hypertension, systemic hypertension, and pulmonary hypertension. Hypoxemia seems to be related either to apnea at the time of intubation or possible airway obstruction associated with positioning.

Bradycardia is presumed to be vagal in origin, because the very rapid onset is suggestive of a reflexive etiology and is not prevented by preoxygenation and the avoidance of hypoxemia. The increase in intracranial pressure may be a result of coughing and struggling of the infant that can result in venous stasis with an increase in cerebral blood volume. Systemic arterial hypertension has been investigated in adults and seems to be caused by an increase in systemic vascular resistance, which is probably caused by catecholamine release.

Pulmonary hypertension leading to right ventricular failure has been described in adults, and although pulmonary artery pressures have not been measured in newborn infants undergoing intubation, endotracheal suctioning is known to cause an increase in pulmonary artery pressure postoperatively in infants with congenital heart disease and is presumed to occur with intubation. In addition, improperly performed direct laryngoscopy can cause traumatic injuries to the face, eyes, tongue, and gums, and placement of the endotracheal tube can dislodge the arytenoids or damage other glottic structures. These injuries can be avoided by improved technique that can be enhanced by the use of premedication.

Characteristics Of An Ideal Strategy

An ideal strategy for premedication for intubation eliminates the pain, discomfort, and physiologic abnormalities of the procedure, helps to carry out intubation expeditiously, minimizes the chances for traumatic injury to the newborn, and has no adverse effects. An individual skilled in the use of bag-mask ventilation should be present to ensure adequate ventilation after the use of
premedication and before the intubation. An ideal approach would be to administer supplemental oxygen, as needed, via a properly sized face mask, then a vagolytic agent, followed by analgesic and/or hypnotic medications before infusion of a muscle relaxant. The vagolytic drug prevents bradycardia, the analgesic and/or hypnotic drug can control pain and may render the infant unconscious and minimize adverse hemodynamic responses to laryngoscopy, and the muscle relaxant provides the best possible intubating conditions. Nonpharmacologic interventions, including swaddling and comfortable positioning, would contribute to the infant’s comfort as well.

**Analgesia**

Premedication with an analgesic reduces the pain and discomfort of intubation. An ideal analgesic agent would have a rapid onset, be of short duration, have no adverse effects on respiratory mechanics, and possess predictable pharmacokinetic properties. None of the currently available agents fit this profile.

Opioids are the most commonly used medications for analgesia in the neonate. The mechanism of action of the individual opioids involves interaction at various receptor sites in both the central and peripheral nervous system to modify transmission of painful signals and diminish pain perception.

Morphine is the most frequently used opiate for pain control in the neonate. It has been used for acute postoperative pain control and as a continuous infusion for ventilated infants. The use of morphine for premedication for intubation was studied in a randomized, controlled trial of 34 premature infants in which infants were given either morphine alone or placebo 5 minutes before the intubation. There was no effect on the severity of physiologic disturbances during intubation including the duration of severe hypoxemia, incidence of bradycardia, and change in mean blood pressure. This lack of effect is thought to be because of the delayed onset of action of morphine related to the relative hydrophilic nature of the drug. Intravenous morphine has a mean
onset of action at 5 minutes and peak effect at 15 minutes. Another randomized, controlled trial of 20 preterm infants compared the use of morphine and midazolam versus remifentanil and midazolam for intubation. No differences were noted between the groups with regard to pain control or hemodynamic variables, but the probability of having excellent intubation conditions was significantly higher with remifentanil than with morphine. All infants pretreated with remifentanil and midazolam were intubated at first attempt compared with only 60% of the infants in the morphine and midazolam group. In another study, when morphine was used in combination with a vagolytic and a paralytic agent, the time needed to intubate was reduced and bradycardia was decreased. However, these effects may be related to the vagolytic and paralytic agents used in the study, not to morphine effects. Furthermore, the status of pain control was not assessed in that study. For these reasons, morphine alone would not be the most appropriate choice for premedication for intubations. Meperidine is rarely used in neonates because of its slow onset of action, variability in metabolism, and risk of toxic effects of its metabolites; as a result, it is not recommended.

Fentanyl is the most frequently used synthetic opioid in the neonate. This drug may be preferable to morphine for pain control for intubation because of a more rapid onset of action related to its more lipophilic nature. Fentanyl’s impact on some of the physiologic disturbances during intubation has been studied. In older infants and children this drug blunts physiologic disturbances during endotracheal suctioning and, in patients after surgery, decreases pulmonary arterial pressure and systemic hypertension. It is likely that such responses may occur during intubation too. Its impact on cerebral and systemic hemodynamics was studied with a short-term infusion in 15 preterm infants, and there were no significant changes in the systemic or cerebral perfusion or pressure. Although fentanyl as a single agent in intubation has not been studied, a cohort study of 33 preterm and term infants intubated after a combination of atropine, fentanyl, and a paralytic
agent showed that fentanyl had no significant adverse effects. Remifentanil, another synthetic opiate, has a rapid onset of action and an ultrashort duration of action and has been shown to be a useful drug for neonatal intubation. A primary concern with synthetic opioid use is the risk of chest wall rigidity, but this risk can be reduced by slow administration and can be treated with either naloxone or muscle relaxants. However, it is important to remember that the use of naloxone, a competitive antagonist at all opioid receptors, will also reverse the analgesic effects of these drugs.

Sedation

Sedatives do not always reduce pain but can sedate or render individuals unconscious or amnestic depending on the dose and individual response. Benzodiazepines have been frequently used for sedation before elective intubations but may not be appropriate in many cases. Midazolam is the most commonly used medication in this category in the United States, but it has not been shown to reduce any physiologic changes during intubation.

In a randomized, double-blind trial (stopped after only 16 intubations because of adverse events and reported in a letter to the editor), preterm infants who received midazolam and atropine for intubation had more desaturations, and 29% required cardiopulmonary resuscitation compared with those in the groups that received either atropine alone or no premedication. Midazolam can cause hypotension in both preterm and term infants, decreased cardiac output in older children, and decreased cerebral blood flow velocity in premature infants.

The studies that demonstrated these effects were not performed as part of premedication for intubation, and the results may not be applicable to the circumstances necessitating endotracheal intubation. However, kinetic studies in preterm and term infants have shown that the serum half-life of midazolam given as continuous infusion or by repetitive dosing can exceed 22 hours. Further concern in the use of midazolam for preterm infants is the
Neonatal Intubation (Specific Considerations)

exposure to the preservative benzyl alcohol. For these reasons, midazolam should not be used in preterm infants, but it can be considered for use in the term or older infant as part of the premedication sequence for elective intubation in the NICU.

Elective intubation of patients before surgery is often accomplished with a sedative-hypnotic agent such as a barbiturate and a muscle relaxant. Barbiturates have been used for induction of anesthesia for decades; however, barbiturates are poor analgesics. Barbiturates such as thiopental and methohexital have a rapid onset and short duration of action. In a randomized, placebo-controlled trial in term infants, thiopental was shown to reduce changes in heart rate and blood pressure during intubation and to shorten the time to intubation. In a small cohort study of term and preterm infants, methohexital facilitated intubation with rapid onset within 1 minute of sedation and recovery within 10 minutes. However, more studies are necessary before methohexital can be recommended for use.

Propofol is a nonbarbiturate anesthetic that is frequently used for induction of anesthesia in older children and adults but has not been well evaluated in newborns. Propofol is lipophilic and rapidly equilibrates between plasma and brain with quick loss of consciousness and also has a short duration of action after a single-bolus dose. In a randomized, controlled trial in 63 premature infants, propofol was shown to be a more effective induction agent than the morphine, atropine, and suxamethonium regimen to facilitate neonatal intubation. Oxygenation during intubation was maintained better in the propofol group and was attributed to the maintenance of spontaneous respiration in infants who received propofol. Twenty-three percent of the infants in the morphine, atropine, and suxamethonium group and 6% of the infants in the propofol group sustained intubation-related trauma. No other adverse events were noted in the propofol group. Although the results of this study are encouraging, more research confirming these initial findings is necessary before propofol can be recommended as a single premedication agent for neonatal
intubation. Propofol can only be administered intravenously, and pain at the site of injection that may sometimes be moderately severe has been reported with intravenous injection of propofol in 10% to 20% of patients.

**Vagolytic Agents**

Vagolytic agents prevent bradycardia during intubation and decrease bronchial and salivary secretions but are infrequently used for neonatal intubation. One reason for their sparse use has been the concern that vagolytic agents mask hypoxia-induced bradycardia during intubation; however, most episodes of bradycardia during intubation are secondary to vagal stimulation, not hypoxia. Glycopyrrolate and atropine are both effective vagolytic agents, and although they have not been directly compared in neonates, they have been studied in infants and children. In a randomized, controlled trial in 90 older infants and children that compared the use of glycopyrrolate and atropine at anesthetic induction, none had bradycardia, but more subjects who received atropine developed sinus tachycardia than those who received glycopyrrolate. Glycopyrrolate is widely used in pediatric intensive care and anesthesia; however, its pharmacokinetics in small preterm infants is not known.

**Muscle Relaxants**

The ideal muscle relaxant for intubation would have a rapid onset, short duration of action, and minimal or no deleterious effect on heart rate and blood pressure. None of the currently available agents meet all these criteria for neonates, but use of a muscle relaxant to facilitate intubation can eliminate or minimize the increase in intracranial pressure that occurs during awake intubation. This has been demonstrated with both succinylcholine in preterm infants and pancuronium in preterm and term infants.

Succinylcholine, the only depolarizing agent in clinical use, blocks neuromuscular transmission by binding to the acetylcholine receptors of the muscle membrane and depolarizing the membrane.
Neonatal Intubation (Specific Considerations)

It has both a rapid onset and a short duration of action. In a randomized, controlled trial in preterm infants, succinylcholine given with morphine and atropine was compared with awake intubation. This combination resulted in faster intubation with less bradycardia and less trauma as defined by less blood in the oral and nasal passages.

The nondepolarizing muscle relaxants compete with acetylcholine for receptors on the motor endplate but do not result in depolarization of the membrane. Of these agents, pancuronium is widely used in newborns and has few adverse effects but is slower in onset of action and longer acting compared with the other available muscle relaxants. Pancuronium has a vagolytic effect that helps minimize the reflex bradycardia that often accompanies laryngoscopy. In a randomized, controlled trial, infants who received pancuronium and atropine showed less hypoxia during intubation and less increase in intracranial pressure compared with infants who received no premedication or atropine alone.

Mivacurium, another nondepolarizing agent, is no longer commercially available because of its adverse effect of histamine release and associated bronchospasm. Cisatracurium has been introduced to replace mivacurium and seems to have similar physiologic effects but has not yet been tested in a neonatal population. Vecuronium and rocuronium, 2 other nondepolarizing muscle relaxants in wide use in pediatric anesthesia and PICUs, are characterized by their minimal effects on blood pressure or heart rate. Rocuronium is a metabolic derivative of vecuronium and has quicker onset to paralysis and shorter duration of action compared with vecuronium.

ENDOTRACHEAL TUBE SUCTION OF VENTILATED NEONATES

Endotracheal intubation prevents the cough reflex and interferes with normal muco-ciliary function, therefore increasing airway secretion production and decreasing the ability to clear
secretions. Endotracheal tube (ETT) suction is necessary to clear secretions and to maintain airway patency, and to therefore optimise oxygenation and ventilation in a ventilated patient.

ETT suction is a common procedure carried out on intubated infants. The goal of ETT suction should be to maximise the amount of secretions removed with minimal adverse effects associated with the procedure.

**Aim**

The aim of the guideline is to outline the principles of management for infants requiring ETT suction for clinicians on Butterfly Ward at the Royal Children’s Hospital.

**Definition of Terms**

- **Endotracheal Tube (ETT):** An airway catheter inserted into the trachea (windpipe) via the mouth or nose in endotracheal intubation. On Butterfly Ward this is usually un-cuffed
- **Endotracheal Intubation:** The placement of a tube into the trachea in order to maintain an open airway in patients who are unable to breathe on their own or maintain their own airway
- **ETT Suction:** The process of applying a negative pressure to the distal ETT or trachea by introducing a catheter to clear excess, or abnormal, secretions
- **PIP:** Peak inspiratory pressure
- **HFOV:** High frequency oscillation ventilation
- **HFJV:** High frequency jet ventilation

**Assessment**

ETT suction should be based on a clinical assessment of the infant. The inspired gas is warmed and humidified (therefore decreasing the risk of secretions drying and occluding the airway).

Auscultate with stethoscope before and after ETT suction to evaluate necessity and effectiveness of the procedure.
Monitor the infant closely before, during and after the procedure to assess baseline, acute physiological changes and recovery. Parameters to observe:

- Oxygen saturation
- Heart rate
- Respiratory rate
- Blood pressure (where possible)
- ETT CO$_2$ or transcutaneous CO$_2$
- Respiratory function monitoring (during conventional modes of ventilation), including flow, pressure, tidal volume and minute volume

Clinical Indications for ETT suction

- Desaturations
- Bradycardia
- Tachycardia
- Absent or decreased chest movement
- Visible secretions in ETT
- Increased ETT CO$_2$ or transcutaneous CO$_2$
- Irritability
- Coarse or decreased breath sounds
- Increased work of breathing
- Blood pressure fluctuations
- Recent history of large amounts of thick / tenacious secretions

Effectiveness of ETT suction should be assessed after the procedure by observing:

- Improvement in breath sounds
- Removal of secretions
- Improved oxygen saturation, transcutaneous CO$_2$, heart rate, blood pressure, respiratory rate
- Decreased work of breathing, improved chest movement.
MEASUREMENT OF LENGTH TO SUCTION

Suction should only be to the tip of the ETT, and should never exceed more than 0.5cm beyond the tip of the ETT, to prevent mucosal irritation and injury.

Measurement of length to suction is to be predetermined at shift commencement. Length is determined by using the centimetre markings on the ETT; and by adding the length of additional space of the ETT adapter (usually 1-1.5 cm). If patient on HFOV or HFJV, allow for different lengths of suction adaptors.

Management

Equipment
- Functioning wall suction unit with suction tubing connected (checked at shift commencement)
- Neopuff set to appropriate settings (checked at shift commencement)
- Suction catheter
- Non sterile gloves
- Normal saline ampoule and 2 ml syringe (if normal saline lavage required)

Procedure
- Where possible, this procedure requires two clinicians. If clinician deems it necessary, she/he may undertake the procedure without assistance and in this situation should alert other nearby members of staff that ETT suction is occurring.
- Explain to parents what is about to occur.
- To determine suction catheter size:

<table>
<thead>
<tr>
<th>ETT Size (mm)</th>
<th>Suction Catheter Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5</td>
<td>5 FG</td>
</tr>
<tr>
<td>3.0 - 3.5</td>
<td>6 - 7 FG</td>
</tr>
<tr>
<td>4.0 - 4.5</td>
<td>8 FG</td>
</tr>
</tbody>
</table>
o Set the suction pressure at -80-100 cmH₂O. Suction pressure may be lower for a small or unstable infant, or higher to remove thick or tenacious secretions. Maximum pressure should not be higher than -200 cmH₂O.

o Pre-silence alarms.

o Primary clinician performs hand hygiene, dons gloves on both hands and protecting key parts attaches appropriate sized suction catheter to suction tubing. Ensuring that the suction catheter does not touch anything that could contaminate it e.g. bed linen.

o Observe pre-suction physiological parameters.

o When the primary clinician and assistant are ready, assistant disconnects ETT from ventilator tubing at ETT adaptor. For HFOV and HFJV use the suction port at the end of the ETT (closed suction) unless otherwise ordered by the medical staff.

o Primary clinician passes suction catheter to predetermined length, ensuring catheter is only passed the length of the ETT.

o Applying negative pressure, primary clinician gently rotates suction catheter as it is being withdrawn from the ETT
  - Negative pressure should only be applied when the suction catheter is being withdrawn from the ETT. For infants on HFJV see Special Considerations for suction procedure recommendatio
  - Duration of negative pressure should not exceed 6 seconds to prevent hypoxaemia
  - Repetitive catheter passes are not used unless the volume of secretions indicates another pass, or the clinician determines another pass is necessary

o To prevent accidental extubation, assistant gently holds infant’s head in steady position and holds ETT steady while primary clinician suctions ETT.
Pediatric and Neonatal Mechanical Ventilation

- Assistant reconnects ventilator tubing to ETT when ETT suction complete, and continues to provide containment and comfort to the infant.
- Allow the infant to rest prior to oropharyngeal and nasopharyngeal suction. The primary clinician suctions infant’s oropharynx and nasopharynx. Oropharyngeal and nasopharyngeal suction allows removal of secretions which accumulate in the oropharynx and nasopharynx. A size 8 or 10 FG tube may be used to suction the oropharynx.
- Observe infant’s post-suction physiological parameters.
- Use a small amount of sterile water if needed to clear secretions from suction tubing.
- Turn off vacuum pressure. Dispose of contaminated catheter, remove gloves and perform hand hygiene.
- Adjust ventilator settings to pre-suctioning baseline (if settings have been adjusted) when indicated by stabilisation of infant’s oxygen saturations and heart rate.
- Ensure infant is left in a contained and comfortable position.
- Document effectiveness of and tolerance to suctioning.
- If the infant requires ETT suction, and a second clinician is unable to assist, the procedure is as above, however the primary clinician will need to detach the ETT from the ventilator with one hand, steady the tube using the same hand and insert the catheter to predetermined length using “clean” hand. Care is especially required to steady the ETT and infant’s head to ensure the infant does not accidentally self-extubate.

Normal Saline Lavage with ETT Suction

Lavage by instillation of normal saline into the ETT immediately prior to ETT suction:

- May aid in the removal of thick, tenacious secretions by thinning, loosening and dislodging these secretions
- Makes the infant cough, which may loosen and dislodge secretions
May lubricate the ET
May have detrimental effects on the infant – damages airway mucosa, acts as a foreign body, does not lead to effective cough as the glottis remains closed in an intubated patient, contributes to lower airway colonisation

Normal saline should not be routinely instilled prior to ETT suction in infants. It should only be instilled in infants who have thick, tenacious secretions. The amount of normal saline to use is 0.1-0.2 ml/kg.

**Oxygenation Pre/Post-Suction**

Oxygenation pre/post suction should not be routine but:
- May reduce the incidence of suction related hypoxaemia and bradycardia
- May cause hyperoxaemia which is associated with oxygen free-radical damage and retinopathy of prematurity

Each infant should be assessed individually regarding whether this is necessary. This is determined by the infant’s clinical condition, response to ETT suction, and length of time it takes for the infant to recover post suction. Care should be taken to ensure the infant’s FiO$_2$ is reduced to baseline as soon as possible after ETT suction.

FiO$_2$ is increased 10-20% above baseline for approximately two minutes prior to suction, and continues after suction is complete until the infant returns to the pre-suction oxygen saturation level.

If the infant’s pre-suction oxygenation is hypoxic, or if the infant becomes severely hypoxic and bradycardic with ETT suction, 100% oxygen may be used prior to ETT suction. This should be decreased as soon as possible after suction is complete.

**Recruitment Post-Suction**

Recruitment post-suction should not be routine, but:
- May reduce atelectasis related to suction and restore functional residual capacity (FRC) after suctioning.
Hyperinflation is achieved by increasing the tidal volume (increasing PIP)

- May result in pneumothorax due to poor or rapidly changing alveolar compliance

Each infant should be assessed individually regarding whether this is necessary. This is determined by the infant’s response to ETT suction, and length of time it takes for the infant to recover post suction.

Using the ventilator setting, PIP is increased 10-20% above baseline for approximately two minutes after suction is complete, or until the infant returns to the pre-suction oxygen saturation level.

For infants being ventilated in TTV+ mode it may also be necessary to increase the set tidal volume by 1 ml/kg if no change in delivered PIP occurs. Care should be taken to ensure the PIP is reduced to baseline as soon as possible after ETT suction. If the oxygen saturations are not improving in the two minutes after suction increasing the PEEP by 1 cmH₂O should be discussed with the Medical Staff.

For infants on HFOV, mean airway pressure is increased 2 cmH₂O above baseline for approximately two minutes after suction is complete, or until the infant returns to the pre-suction oxygen saturation level. Care should be taken to ensure the mean airway pressure is reduced to baseline as soon as possible after ETT suction.

For infants on HFJV the back up conventional rate should be increased by 1-2 inflations per minute for approximately two minutes after suction is complete, or until the infant returns to the pre-suction oxygen saturation level.

**Hyperventilation Pre-Suction**

Hyperventilation pre-suction should not be routine, but:

- May reduce hypoxaemia related to suction and shorten stabilisation and recovery times
Each infant should be assessed individually regarding whether hyperventilation pre-suction is necessary. This is determined by the infant’s response to ETT suction, and length of time it takes for the infant to recover post suction.

Using the ventilator setting, rate is increased by 5-10 breaths above baseline immediately prior to suction, and continues after suction is complete until the infant returns to the pre-suction oxygen saturation and ETT or transcutaneous CO₂ level. Care should be taken to ensure the rate is reduced to baseline as soon as possible after ETT suction.

For infants on HFJV, conventional ventilator rate may be increased by 1-2 breaths above baseline immediately prior to suction, and continues after suction is complete until the infant returns to the pre-suction oxygen saturation and transcutaneous CO₂ level. Care should be taken to ensure the rate is reduced to baseline as soon as possible after ETT suction.

Complications of ETT suction
- Hypoxaemia
- Atelectasis
- Bradycardia
- Tachycardia
- Increased ETT CO₂ and transcutaneous CO₂
- Blood pressure fluctuations
- Decreased tidal volume
- Airway mucosal trauma
- ETT dislodgement
- Pneumothorax
- Pneumomediastinum
- Bacteraemia
- Pneumonia
- Fluctuations in intracranial pressure and cerebral blood flow velocity
Complications of oropharyngeal and nasopharyngeal suction:
  - Hypoxia
  - Bradycardia

**Documentation**

Document clearly in EMR:
  - ETT suctioned
  - Airway secretion amount
  - Airway secretion colour
  - Suction tolerance
  - Significant events

**Family Centred Care**

It is the responsibility of the clinician caring for the infant requiring ETT suction to ensure that the parents understand the rationale for the procedure, as well as potential complications.

**SPECIAL CONSIDERATIONS**

**Analgesia/Sedation**

Some infants may require a pre-suction bolus of analgesia or sedation where the need is anticipated, however urgent suction should not be deferred. The need for this intervention is based on clinical assessment.

**Open Suction for HFOV and HFJV**

Most infants on HFOV and HFJV have in-line suction connected to the circuit. Open suction may be indicated for infants on HFOV and HFJV, as this can result in more effective removal of thick secretions. The need for this intervention is not routine, and where appropriate should be ordered by medical staff.

**Infection Control**

Use aseptic technique and personal protective equipment.
Patient Safety

Where possible, ETT suction is a 2 person procedure. The primary clinician suctions the ETT maintaining infection control precautions. The assistant ensures the infant remains safe from accidental extubation, adjusts ventilator settings if necessary, and provides containment and comfort to the infant.
Oxygen Supplementation, Delivery and Physiologic Effects

OXYGEN THERAPY

Oxygen therapy is the administration of oxygen as a medical intervention, which can be for a variety of purposes in both chronic and acute patient care.

Normal air is composed of 20.95% oxygen by volume; it is essential for cell metabolism, and in turn, tissue oxygenation is essential for all normal physiological functions.

High blood and tissue levels of oxygen can be helpful or damaging, depending on circumstances. Oxygen therapy is used when low blood oxygen is present. Oxygen may be administered in various ways from a nasal cannula to hyperbaric oxygen inside a closed chamber.

Medical uses

Oxygen is used as a medical treatment in both chronic and acute cases, and can be used in hospital, pre-hospital or entirely out of hospital, dependent on the needs of the patient and their medical professionals’ opinions.
**Oxygen Supplementation, Delivery and Physiologic Effects**

**Chronic conditions**

A common use of supplementary oxygen is in patients with chronic obstructive pulmonary disease (COPD), the occurrence of chronic bronchitis or emphysema, a common long-term effect of smoking, who may require additional oxygen to breathe either during a temporary worsening of their condition, or throughout the day and night. It is indicated in COPD patients with $\text{PaO}_2 < 55$ mmHg (7.3 kPa) or $\text{SaO}_2 < 88\%$ and has been shown to increase lifespan.

Oxygen is often prescribed for people with breathlessness, in the setting of end-stage cardiac or respiratory failure, advanced cancer or neurodegenerative disease, despite having relatively normal blood oxygen levels. A 2010 trial of 239 subjects found no significant difference in reducing breathlessness between oxygen and air delivered in the same way.

**Acute conditions**

Oxygen is widely used in emergency medicine, both in hospital and by emergency medical services or those giving advanced first aid.

In the pre-hospital environment, high flow oxygen is definitively indicated for use in resuscitation, major trauma, anaphylaxis, major haemorrhage, shock, active convulsions and hypothermia.

It may also be indicated for any other patient where their injury or illness has caused hypoxaemia, although in this case oxygen flow should be moderated to achieve target oxygen saturation levels, based on pulse oximetry (with a target level of 94–98% in most patients, or 88–92% in COPD patients).

For personal use, high concentration oxygen is used as home therapy to abort cluster headache attacks, due to its vasoconstrictive effects.

Patients who are receiving oxygen therapy for hypoxemia following an acute illness or hospitalization should not routinely
have a prescription renewal for continued oxygen therapy without a physician’s re-assessment of the patient’s condition. If the person has recovered from the illness, then the hypoxemia is expected to resolve and additional care would be unnecessary and a waste of resources.

**Side effects**

Many EMS protocols indicate that oxygen should not be withheld from any patient, while other protocols are more specific or circumspect. However, there are certain situations in which oxygen therapy is known to have a negative impact on a patient’s condition.

Oxygen should never be given to a patient who is suffering from paraquat poisoning unless they are suffering from severe respiratory distress or respiratory arrest, as this can increase the toxicity. (Paraquat poisoning is rare — for example 200 deaths globally from 1958 to 1978). Oxygen therapy is not recommended for patients who have suffered pulmonary fibrosis or other lung damage resulting from bleomycin treatment.

High levels of oxygen given to infants causes blindness by promoting overgrowth of new blood vessels in the eye obstructing sight. This is retinopathy of prematurity (ROP).

Oxygen has vasoconstrictive effects on the circulatory system, reducing peripheral circulation and was once thought to potentially increase the effects of stroke. However, when additional oxygen is given to the patient, additional oxygen is dissolved in the plasma according to Henry’s Law. This allows a compensating change to occur and the dissolved oxygen in plasma supports embarrassed (oxygen-starved) neurons, reduces inflammation and post-stroke cerebral edema. Since 1990, hyperbaric oxygen therapy has been used in the treatments of stroke on a worldwide basis. In rare instances, hyperbaric oxygen therapy patients have had seizures. However, because of the aforementioned Henry’s Law effect of extra available dissolved oxygen to neurons, there is usually no negative sequel to the event. Such seizures are generally a result
Oxygen Supplementation, Delivery and Physiologic Effects

of oxygen toxicity, although hypoglycemia may be a contributing factor, but the latter risk can be eradicated or reduced by carefully monitoring the patient’s nutritional intake prior to oxygen treatment.

Oxygen first aid has been used as an emergency treatment for diving injuries for years. Recompression in a hyperbaric chamber with the patient breathing 100% oxygen is the standard hospital and military medical response to decompression illness. The success of recompression therapy as well as a decrease in the number of recompression treatments required has been shown if first aid oxygen is given within four hours after surfacing. There are suggestions that oxygen administration may not be the most effective measure for the treatment of decompression illness and that heliox may be a better alternative.

Chronic obstructive pulmonary disease

Care needs to be exercised in patients with chronic obstructive pulmonary disease, such as emphysema, especially in those known to retain carbon dioxide (type II respiratory failure). Such patients may further accumulate carbon dioxide and decreased pH (hypercapnation) if administered supplemental oxygen, possibly endangering their lives. This is primarily as a result of ventilation-perfusion imbalance. In the worst case, administration of high levels of oxygen in patients with severe emphysema and high blood carbon dioxide may reduce respiratory drive to the point of precipitating respiratory failure, with an observed increase in mortality compared with those receiving titrated oxygen treatment. However, the risk of the loss of respiratory drive are far outweighed by the risks of withholding emergency oxygen, and therefore emergency administration of oxygen is never contraindicated. Transfer from field care to definitive care, where oxygen use can be carefully calibrated, typically occurs long before significant reductions to the respiratory drive.

A 2010 study has shown that titrated oxygen therapy (controlled administration of oxygen) is less of a danger to COPD
patients and that other, non-COPD patients, may also, in some cases, benefit more from titrated therapy.

Fire risk

Highly concentrated sources of oxygen promote rapid combustion. Oxygen itself is not flammable, but the addition of concentrated oxygen to a fire greatly increases its intensity, and can aid the combustion of materials (such as metals) which are relatively inert under normal conditions. Fire and explosion hazards exist when concentrated oxidants and fuels are brought into close proximity; however, an ignition event, such as heat or a spark, is needed to trigger combustion. A well-known example of an accidental fire accelerated by pure oxygen under pressure occurred in the Apollo 1 spacecraft in January 1967 during a ground test; it killed all three astronauts. A similar accident killed Soviet cosmonaut Valentin Bondarenko in 1961.

Combustion hazards also apply to compounds of oxygen with a high oxidative potential, such as peroxides, chlorates, nitrates, perchlorates, and dichromates because they can donate oxygen to a fire.

Concentrated O2 will allow combustion to proceed rapidly and energetically. Steel pipes and storage vessels used to store and transmit both gaseous and liquid oxygen will act as a fuel; and therefore the design and manufacture of O2 systems requires special training to ensure that ignition sources are minimized. Highly concentrated oxygen in a high-pressure environment can spontaneously ignite hydrocarbons such as oil and grease, resulting in fire or explosion. The heat caused by rapid pressurization serves as the ignition source. For this reason, storage vessels, regulators, piping and any other equipment used with highly concentrated oxygen must be “oxygen-clean” prior to use, to ensure the absence of potential fuels. This does not apply only to pure oxygen; any concentration significantly higher than atmospheric (approximately 21%) carries a potential risk.
Hospitals in some jurisdictions, such as the UK, now operate “no-smoking” policies, which although introduced for other reasons, supports the aim of keeping ignition sources away from medical piped oxygen. Other recorded sources of ignition of medically prescribed oxygen include candles, aromatherapy, medical equipment, cooking, and unfortunately, deliberate vandalism. Smoking pipes, cigars and cigarettes are of special concern. This does not entirely eliminate the risk of injury with portable oxygen systems, especially if compliance is poor.

**Alternative medicine**

Some practitioners of alternative medicine have promoted “oxygen therapy” as a cure for many human ailments including AIDS, Alzheimer’s disease and cancer. The procedure may include injecting hydrogen peroxide, oxygenating blood, or administering oxygen under pressure to the rectum, vagina, or other bodily opening. According to the American Cancer Society, “available scientific evidence does not support claims that putting oxygen-releasing chemicals into a person’s body is effective in treating cancer”, and some of these treatments can be dangerous.

**STORAGE AND SOURCES**

Oxygen can be separated by a number of methods, including chemical reaction and fractional distillation, and then either used immediately or stored for future use. The main types sources for oxygen therapy are:

1. **Liquid storage** — Liquid oxygen is stored in chilled tanks until required, and then allowed to boil (at a temperature of 90.188 K (−182.96 °C)) to release oxygen as a gas. This is widely used at hospitals due to their high usage requirements, but can also be used in other settings.

2. **Compressed gas storage** — The oxygen gas is compressed in a gas cylinder, which provides a convenient storage, without the requirement for refrigeration found with liquid storage. Large oxygen cylinders hold 6,500 litres (230 cu ft)
and can last about two days at a flow rate of 2 litres per minute. A small portable M6 (B) cylinder holds 164 or 170 litres (5.8 or 6.0 cu ft) and weighs about 1.3 to 1.6 kilograms (2.9 to 3.5 lb). These tanks can last 4-6 hours when used with a conserving regulator, which senses the patient’s breathing rate and sends pulses of oxygen. Conserving regulators may not be usable by patients who breathe through their mouths.

3. Instant usage — The use of an electrically powered oxygen concentrator or a chemical reaction based unit can create sufficient oxygen for a patient to use immediately, and these units (especially the electrically powered versions) are in widespread usage for home oxygen therapy and portable personal oxygen, with the advantage of being continuous supply without the need for additional deliveries of bulky cylinders.

Delivery

Various devices are used for administration of oxygen. In most cases, the oxygen will first pass through a pressure regulator, used to control the high pressure of oxygen delivered from a cylinder (or other source) to a lower pressure. This lower pressure is then controlled by a flowmeter, which may be preset or selectable, and this controls the flow in a measure such as litres per minute (lpm). The typical flowmeter range for medical oxygen is between 0 and 15 lpm with some units able to obtain up to 25 liters per minute. Many wall flowmeters using a Thorpe tube design are able to be dialed to “flush” which is beneficial in emergency situations.

Supplemental oxygen

Many patients require only a supplementary level of oxygen in the room air they are breathing, rather than pure or near pure oxygen, and this can be delivered through a number of devices dependent on the situation, flow required and in some instances patient preference.
A nasal cannula (NC) is a thin tube with two small nozzles that protrude into the patient’s nostrils. It can only comfortably provide oxygen at low flow rates, 2–6 litres per minute (LPM), delivering a concentration of 24–40%.

There are also a number of face mask options, such as the simple face mask, often used at between 5 and 8 LPM, with a concentration of oxygen to the patient of between 28% and 50%. This is closely related to the more controlled air-entrainment masks, also known as Venturi masks, which can accurately deliver a predetermined oxygen concentration to the trachea up to 40%.

In some instances, a partial rebreathing mask can be used, which is based on a simple mask, but featuring a reservoir bag, which increases the provided oxygen concentration to 40–70% oxygen at 5 to 15 LPM.

Non-rebreather masks draw oxygen from attached reservoir bags, with one-way valves that direct exhaled air out of the mask. When properly fitted and used at flow rates of 8-10 LPM or higher, they deliver close to 100% oxygen. This type of mask is indicated for acute medical emergencies.

Demand oxygen delivery systems (DODS) or oxygen resuscitators deliver oxygen only when the person inhales, or, in the case of an non-breathing people, the caregiver presses a button on the mask.

These systems greatly conserve oxygen compared to steady-flow masks, which is useful in emergency situations when a limited supply of oxygen is available and there is a delay in transporting the patient to higher care.

They are very useful in performing CPR, as the caregiver can deliver rescue breaths composed of 100% oxygen with the press of a button. Care must be taken not to over-inflate the patient’s lungs, and some systems employ safety valves to help prevent this. These systems may not be appropriate for unconscious patients or those in respiratory distress, because of the effort required to breathe from them.
High flow oxygen delivery

In cases where the patient requires a high concentration of up to 100% oxygen, a number of devices are available, with the most common being the non-rebreather mask (or reservoir mask), which is similar to the partial rebreathing mask except it has a series of one-way valves preventing exhaled air from returning to the bag. There should be a minimum flow of 10 L/min. The delivered FIO2 of this system is 60-80%, depending on the oxygen flow and breathing pattern. Another type of device is a humidified high flow nasal cannula which enables flows exceeding a patient’s peak inspiratory flow demand to be delivered via nasal cannula, thus providing FiO2 of up to 100% because there is no entrainment of room air, even with the mouth open. This also allows the patient to continue to talk, eat and drink while still receiving the therapy. This type of delivery method is associated with greater overall comfort, and improved oxygenation and respiratory rates than with face mask oxygen.

In specialist applications such as aviation, tight fitting masks can be used, and these also have applications in anaesthesia, carbon monoxide poisoning treatment and in hyperbaric oxygen therapy.

Positive pressure delivery

Patients who are unable to breathe on their own will require positive pressure to move oxygen into their lungs for gaseous exchange to take place. Systems for delivering this vary in complexity (and cost), starting with a basic pocket mask adjunct which can be used by a basically trained first aider to manually deliver artificial respiration with supplemental oxygen delivered through a port in the mask.

Many emergency medical service and first aid personnel, as well as hospitals, will use a bag-valve-mask (BVM), which is a malleable bag attached to a face mask (or invasive airway such as an endotracheal tube or laryngeal mask airway), usually with a reservoir bag attached, which is manually manipulated by the
healthcare professional to push oxygen (or air) into the lungs. This is the only procedure allowed for initial treatment of cyanide poisoning in the UK workplace.

Automated versions of the BVM system, known as a resuscitator or pneupac can also deliver measured and timed doses of oxygen direct to patient through a facemask or airway. These systems are related to the anaesthetic machines used in operations under general anaesthesia that allows a variable amount of oxygen to be delivered, along with other gases including air, nitrous oxide and inhalational anaesthetics.

As a drug delivery route

Oxygen and other compressed gasses are used in conjunction with a nebulizer to allow the delivery of medications to the upper and/or lower airways. Nebulizers use compressed gas to propel liquid medication into an aerosol, with specific therapeutically sized droplets, for deposition in the appropriate, desired portion of the airway. A typical compressed gas flow rate of 8-10 L/min is used to nebulize medications, saline, sterile water, or a mixture of the preceding into a therapeutic aerosol for inhalation. In the clinical setting room air (ambient mix of several gasses), molecular oxygen, and Heli-Ox are the most common gases used to nebulize a bolus or a continuous volume of therapeutic aerosols.

Exhalation filters for oxygen masks

Filtered oxygen masks have the ability to prevent exhaled, potentially infectious particles from being released into the surrounding environment. These masks are normally of a closed design such that leaks are minimized and breathing of room air is controlled through a series of one-way valves. Filtration of exhaled breaths is accomplished either by placing a filter on the exhalation port, or through an integral filter that is part of the mask itself. These masks first became popular in the Toronto (Canada) healthcare community during the 2003 SARS Crisis. SARS was identified as being respiratory based and it was
determined that conventional oxygen therapy devices were not designed for the containment of exhaled particles. Common practices of having suspected patients wear a surgical mask was confounded by the use of standard oxygen therapy equipment. In 2003, the HiOx® oxygen mask was released for sale. The HiOx® mask is a closed design mask that allows a filter to be placed on the exhalation port. Several new designs have emerged in the global healthcare community for the containment and filtration of potentially infectious particles. Other designs include the ISO-O2 oxygen mask, the FloMax® oxygen mask, and the O-Mask. The use of oxygen masks that are capable of filtering exhaled particles is gradually becoming a recommended practice for pandemic preparation in many jurisdictions.

Typical oxygen masks allow the patient to breathe in room air in addition to their therapeutic oxygen, but because filtered oxygen masks use a closed design that minimizes or eliminates the patient’s contact with and ability to inhale room air, delivered oxygen concentrations to the patient have been found to be higher, approaching 99% using adequate oxygen flows. Because all exhaled particles are contained within the mask, nebulized medications are also prevented from being released into the surrounding atmosphere, decreasing the occupational exposure to healthcare staff and other patients.

OXYGEN THERAPY WHILE ON AIRCRAFT

In the United States, most airlines restrict the devices allowed on board aircraft. As a result, passengers are restricted in what devices they can use. Some airlines will provide cylinders for passengers with an associated fee. Other airlines allow passengers to carry on approved portable concentrators. However the lists of approved devices varies by airline so passengers need to check with any airline they are planning to fly on. Passengers are generally not allowed to carry on their own cylinders. In all cases, passengers need to notify the airline in advance of their equipment.
Effective May 13, 2009, the Department of Transportation and FAA ruled that a select number of portable oxygen concentrators are approved for use on all commercial flights.

FAA regulations require larger airplanes to carry D-cylinders of oxygen for use in an emergency.

HYPERBARIC MEDICINE

Hyperbaric medicine is medical treatment in which an ambient pressure greater than sea level atmospheric pressure is a necessary component. The treatment comprises hyperbaric oxygen therapy (HBOT), the medical use of oxygen at an ambient pressure higher than atmospheric pressure, and therapeutic recompression for decompression illness, intended to reduce the injurious effects of systemic gas bubbles by physically reducing their size and providing improved conditions for elimination of bubbles and excess dissolved gas.

The equipment required for hyperbaric oxygen treatment consists of a pressure chamber, which may be of rigid or flexible construction, and a means of delivering 100% oxygen. Operation is performed to a predetermined schedule by trained personnel who monitor the patient and may adjust the schedule as required. HBOT found early use in the treatment of decompression sickness, and has also shown great effectiveness in treating conditions such as gas gangrene and carbon monoxide poisoning. More recent research has examined the possibility that it may also have value for other conditions such as cerebral palsy and multiple sclerosis, but no significant evidence has been found.

Therapeutic recompression is usually also provided in a hyperbaric chamber. It is the definitive treatment for decompression sickness and may also be used to treat arterial gas embolism caused by pulmonary barotrauma of ascent. In emergencies divers may sometimes be treated by in-water recompression if a chamber is not available and suitable diving equipment to reasonably secure the airway is available.
A number of hyperbaric treatment schedules have been published over the years for both therapeutic recompression and hyperbaric oxygen therapy for other conditions.

Scope

Hyperbaric medicine includes hyperbaric oxygen treatment, which is the medical use of oxygen at greater than atmospheric pressure to increase the availability of oxygen in the body; and therapeutic recompression, which involves increasing the ambient pressure on a person, usually a diver, to treat decompression sickness or an air embolism by eliminating bubbles that have formed within the body.

Medical uses

In the United States the Undersea and Hyperbaric Medical Society, known as UHMS, lists approvals for reimbursement for certain diagnoses in hospitals and clinics. The following indications are approved (for reimbursement) uses of hyperbaric oxygen therapy as defined by the UHMS Hyperbaric Oxygen Therapy Committee:

- Air or gas embolism;
- Carbon monoxide poisoning;
  - Carbon monoxide poisoning complicated by cyanide poisoning;
- Central retinal artery occlusion;
- Clostridal myositis and myonecrosis (gas gangrene);
- Crush injury, compartment syndrome, and other acute traumatic ischemias;
- Decompression sickness;
- Enhancement of healing in selected problem wounds;
  - Diabetically derived illness, such as diabetic foot, diabetic retinopathy, diabetic nephropathy;
- Exceptional blood loss (anemia);
- Idiopathic sudden sensorineural hearing loss;
• Intracranial abscess;
• Mucormycosis, especially rhinocerebral disease in the setting of diabetes mellitus;
• Necrotizing soft tissue infections (necrotizing fasciitis);
• Osteomyelitis (refractory);
• Delayed radiation injury (soft tissue and bony necrosis);
• Skin grafts and flaps (compromised);
• Thermal burns.

Evidence is insufficient as of 2013 to support its use in autism, cancer, diabetes, HIV/AIDS, Alzheimer’s disease, asthma, Bell’s palsy, cerebral palsy, depression, heart disease, migraines, multiple sclerosis, Parkinson’s disease, spinal cord injury, sports injuries, or stroke.

A Cochrane review published in 2016 has raised questions about the ethical basis for future clinical trials of hyperbaric oxygen therapy, in view of the increased risk of damage to the eardrum in children with autism spectrum disorders. Despite the lack of evidence, in 2015, the number of people utilizing this therapy has continued to rise.

Hearing issues

There is limited evidence that hyperbaric oxygen therapy improves hearing in patients with sudden sensorineural hearing loss who present within two weeks of hearing loss. There is some indication that HBOT might improve tinnitus presenting in the same time frame.

Chronic ulcers

HBOT in diabetic foot ulcers increased the rate of early ulcer healing but does not appear to provide any benefit in wound healing at long term follow-up. In particular, there was no difference in major amputation rate. For venous, arterial and pressure ulcers, no evidence was apparent that HBOT provides an improvement over standard treatment.
Radiation injury

There is some evidence that HBOT is effective for late radiation tissue injury of bone and soft tissues of the head and neck. Some people with radiation injuries of the head, neck or bowel show an improvement in quality of life. Importantly, no such effect has been found in neurological tissues. The use of HBOT may be justified to selected patients and tissues, but further research is required to establish the best people to treat and timing of any HBO therapy.

Neuro-rehabilitation

There is tentative evidence for HBOT in traumatic brain injury. As of 2012 there is insufficient evidence to support its general use in TBI. In stroke HBOT does not show benefit. HBOT in multiple sclerosis has not shown benefit and routine use is not recommended.

A 2007 review of HBOT in cerebral palsy found no difference compared to the control group. Neuropsychological tests also showed no difference between HBOT and room air and based on caregiver report, those who received room air had significantly better mobility and social functioning. Children receiving HBOT were reported to experience seizures and the need for tympanostomy tubes to equalize ear pressure, though the incidence was not clear.

Cancer

In alternative medicine, hyperbaric medicine has been promoted as a treatment for cancer, but there is no evidence it is effective for this purpose.

CONTRAINDICATIONS

The toxicology of the treatment has recently been reviewed by Ustundag et al. and its risk management is discussed by Christian R. Mortensen, in light of the fact that most hyperbaric facilities are managed by departments of anaesthesiology and some of their patients are critically ill.
The only absolute contraindication to hyperbaric oxygen therapy is untreated pneumothorax. The reason is concern that it can progress to tension pneumothorax, especially during the decompression phase of therapy, although treatment on oxygen-based tables may avoid that progression. The COPD patient with a large bleb represents a relative contraindication for similar reasons. Also, the treatment may raise the issue of Occupational health and safety (OHS), which has been encountered by the therapist. Patients should not undergo HBO therapy if they are taking or have recently taken the following drugs:

- Doxorubicin (Adriamycin) – A chemotherapeutic drug. This drug has been shown to potentiate cytotoxicity during HBO therapy.
- Cisplatin – Also a chemotherapeutic drug.
- Disulfiram (Antabuse) – Used in the treatment of alcoholism.
- Mafenide acetate (Sulfamylon) – Suppresses bacterial infections in burn wounds

The following are relative contraindications — meaning that special consideration must be made by specialist physicians before HBO treatments begin:

- Cardiac disease
- COPD with air trapping - can lead to pneumothorax during treatment.
- Upper respiratory infections – These conditions can make it difficult for the patient to equalise their ears or sinuses, which can result in what is termed ear or sinus squeeze.
- High fevers – In most cases the fever should be lowered before HBO treatment begins. Fevers may predispose to convulsions.
- Emphysema with CO$_2$ retention – This condition can lead to pneumothorax during HBO treatment due to rupture of an emphysematous bulla. This risk can be evaluated by x-ray.
• History of thoracic (chest) surgery – This is rarely a problem and usually not considered a contraindication. However, there is concern that air may be trapped in lesions that were created by surgical scarring. These conditions need to be evaluated prior to considering HBO therapy.

• Malignant disease: Cancers thrive in blood-rich environments but may be suppressed by high oxygen levels. HBO treatment of individuals who have cancer presents a problem, since HBO both increases blood flow via angiogenesis and also raises oxygen levels. Taking an anti-angiogenic supplement may provide a solution. A study by Feldemier, et al. and recent NIH funded study on Stem Cells by Thom, et al., indicate that HBO is actually beneficial in producing stem/progenitor cells and the malignant process is not accelerated.

• Middle ear barotrauma is always a consideration in treating both children and adults in a hyperbaric environment because of the necessity to equalise pressure in the ears.

Pregnancy is not a relative contraindication to hyperbaric oxygen treatments, although it may be for underwater diving. In cases where a pregnant woman has carbon monoxide poisoning there is evidence that lower pressure (2.0 ATA) HBOT treatments are not harmful to the fetus, and that the risk involved is outweighed by the greater risk of the untreated effects of CO on the fetus (neurologic abnormalities or death.) In pregnant patients, HBO therapy has been shown to be safe for the fetus when given at appropriate levels and “doses” (durations). In fact, pregnancy lowers the threshold for HBO treatment of carbon monoxide-exposed patients. This is due to the high affinity of fetal hemoglobin for CO.

Therapeutic principles

The therapeutic consequences of HBOT and recompression result from multiple effects. The increased overall pressure is of therapeutic value in the treatment of decompression sickness and
air embolism as it provides a physical means of reducing the volume of inert gas bubbles within the body; Exposure to this increased pressure is maintained for a period long enough to ensure that most of the bubble gas is dissolved back into the tissues, removed by perfusion and eliminated in the lungs. The improved concentration gradient for inert gas elimination (oxygen window) by using a high partial pressure of oxygen increases the rate of inert gas elimination in the treatment of decompression sickness. For many other conditions, the therapeutic principle of HBOT lies in its ability to drastically increase partial pressure of oxygen in the tissues of the body. The oxygen partial pressures achievable using HBOT are much higher than those achievable while breathing pure oxygen under normobaric conditions (i.e. at normal atmospheric pressure); A related effect is the increased oxygen transport capacity of the blood. Under normal atmospheric pressure, oxygen transport is limited by the oxygen binding capacity of hemoglobin in red blood cells and very little oxygen is transported by blood plasma. Because the hemoglobin of the red blood cells is almost saturated with oxygen under atmospheric pressure, this route of transport cannot be exploited any further. Oxygen transport by plasma, however is significantly increased using HBOT as the stimulus. Recent evidence suggests that exposure to hyperbaric oxygen (HBOT) mobilizes stem/progenitor cells from the bone marrow by a nitric oxide (NO) -dependent mechanism. This mechanism may account for the patient cases that indicate recovery of damaged organs and tissues with HBOT.

**Hyperbaric chambers**

**Construction**

The traditional type of hyperbaric chamber used for therapeutic recompression and HBOT is a rigid shelled pressure vessel. Such chambers can be run at absolute pressures typically about 6 bars (87 psi), 600,000 Pa or more in special cases. Navies, professional diving organizations, hospitals, and dedicated recompression facilities typically operate these. They range in size from semi-
A rigid chamber may consist of:

- a pressure vessel that is generally made of steel or aluminium with the view ports (windows) made of acrylic;
- one or more human entry hatches—small and circular or wheel-in type hatches for patients on gurneys;
- the entry lock that allows human entry—a separate chamber with two hatches, one to the outside and one to the main chamber, which can be independently pressurized to allow patients to enter or exit the main chamber while it is still pressurized.
- a low volume medical or service airlock for medicines, instruments, and food;
- transparent ports or closed-circuit television that allows technicians and medical staff outside the chamber to monitor the patient inside the chamber;
- an intercom system allowing two-way communication;
- an optional carbon dioxide scrubber—consisting of a fan that passes the gas inside the chamber through a soda lime canister;
- a control panel outside the chamber to open and close valves that control air flow to and from the chamber, and regulate oxygen to hoods or masks;
- an over-pressure relief valve.
- a built-in breathing system (BIBS) to supply and exhaust treatment gas.
- a fire suppression system.

Flexible monoplace chambers are available ranging from collapsible flexible aramid fiber-reinforced chambers which can be disassembled for transport via truck or SUV, with a maximum working pressure of 2 bar above ambient complete with BIBS allowing full oxygen treatment schedules to portable, air inflated
“soft” chambers that can operate at between 0.3 and 0.5 bars (4.4 and 7.3 psi) above atmospheric pressure with no supplemental oxygen, and longitudinal zipper closure.

Hard chambers and soft chambers are not equivalent in efficacy and safety as they are different in many aspects.

**Oxygen supply**

In the larger multiplace chambers, patients inside the chamber breathe from either “oxygen hoods” – flexible, transparent soft plastic hoods with a seal around the neck similar to a space suit helmet – or tightly fitting oxygen masks, which supply pure oxygen and may be designed to directly exhaust the exhaled gas from the chamber. During treatment patients breathe 100% oxygen most of the time to maximise the effectiveness of their treatment, but have periodic “air breaks” during which they breathe chamber air (21% oxygen) to reduce the risk of oxygen toxicity. The exhaled treatment gas must be removed from the chamber to prevent the buildup of oxygen, which could present a fire risk. Attendants may also breathe oxygen some of the time to reduce their risk of decompression sickness when they leave the chamber. The pressure inside the chamber is increased by opening valves allowing high-pressure air to enter from storage cylinders, which are filled by an air compressor. Chamber air oxygen content is kept between 19% and 23% to control fire risk (US Navy maximum 25%). If the chamber does not have a scrubber system to remove carbon dioxide from the chamber gas, the chamber must be isobarically ventilated to keep the CO$_2$ within acceptable limits.

A soft chamber may be pressurised directly from a compressor, or from storage cylinders.

Smaller “monoplace” chambers can only accommodate the patient, and no medical staff can enter. The chamber may be pressurised with pure oxygen or compressed air. If pure oxygen is used, no oxygen breathing mask or helmet is needed, but the cost of using pure oxygen is much higher than that of using compressed air. If compressed air is used, then an oxygen mask
or hood is needed as in a multiplace chamber. Most monoplace chambers can be fitted with a demand breathing system for air breaks. In low pressure soft chambers, treatment schedules may not require air breaks, because the risk of oxygen toxicity is low due to the lower oxygen partial pressures used (usually 1.3 ATA), and short duration of treatment.

For alert, cooperative patients, air breaks provided by mask are more effective than changing the chamber gas because they provide a quicker gas change and a more reliable gas composition both during the break and treatment periods.

Treatments

Initially, HBOT was developed as a treatment for diving disorders involving bubbles of gas in the tissues, such as decompression sickness and gas embolism. It is still considered the definitive treatment for these conditions. The chamber treats decompression sickness and gas embolism by increasing pressure, reducing the size of the gas bubbles and improving the transport of blood to downstream tissues. The high concentrations of oxygen in the tissues are beneficial in keeping oxygen-starved tissues alive, and have the effect of removing the nitrogen from the bubble, making it smaller until it consists only of oxygen, which is re-absorbed into the body. After elimination of bubbles, the pressure is gradually reduced back to atmospheric levels. Hyperbaric chambers are also used for animals, especially race horses where a recovery is worth a great deal to their owners. It is also used to treat dogs and cats in pre- and post-surgery treatment to strengthen their systems prior to surgery and then accelerate healing post surgery.

Protocol

The slang term, at some facilities, for a cycle of pressurization inside the HBOT chamber is “a dive”. An HBOT treatment for longer-term conditions is often a series of 20 to 40 dives, or compressions. These dives last for about an hour and can be
administered via a hard, high-pressure chamber or a soft, low-pressure chamber—the major difference being per-dive “dose” of oxygen. Many conditions do quite well with the lower dose, lower cost-per-hour, soft chambers.

Emergency HBOT for decompression illness follows treatment schedules laid out in treatment tables. Most cases employ a recompression to 2.8 bars (41 psi) absolute, the equivalent of 18 metres (60 ft) of water, for 4.5 to 5.5 hours with the casualty breathing pure oxygen, but taking air breaks every 20 minutes to reduce oxygen toxicity. For extremely serious cases resulting from very deep dives, the treatment may require a chamber capable of a maximum pressure of 8 bars (120 psi), the equivalent of 70 metres (230 ft) of water, and the ability to supply heliox as a breathing gas.

U.S. Navy treatment charts are used in Canada and the United States to determine the duration, pressure, and breathing gas of the therapy.

The Undersea and Hyperbaric Medical Society (UHMS) publishes a report that compiles the latest research findings and contains information regarding the recommended duration and pressure of the longer-term conditions.

**Home and out-patient clinic treatment**

There are several sizes of portable chambers, which are used for home treatment. These are usually referred to as “mild personal hyperbaric chambers”, which is a reference to the lower pressure (compared to hard chambers) of soft-sided chambers. Food and Drug Administration (FDA) approved chambers for use with room air are available in the USA and may go up to 4.4 pounds per square inch (psi) above atmospheric pressure, which equals 1.3 atmospheres absolute (ATA), equivalent to a depth of 10 feet of sea water. In the US, these “mild personal hyperbaric chambers” are categorized by the FDA as CLASS II medical devices and requires a prescription in order to purchase one or take treatments. Personal hyperbaric chambers are only FDA approved to reach
1.3 ATA. While hyperbaric chamber distributors and manufacturers cannot supply a chamber in the US with any form of elevated oxygen delivery system, a physician can write a prescription to combine the two modalities, as long as there is a prescription for both hyperbarics and oxygen.

The most common option (but not approved by FDA) some patients choose is to acquire an oxygen concentrator which typically delivers 85–96% oxygen as the breathing gas. Because of the high circulation of air through the chamber, the total concentration of oxygen in the chamber never exceeds 25% as this can increase the risk of fire. Oxygen is never fed directly into soft chambers but is rather introduced via a line and mask directly to the patient. FDA approved oxygen concentrators for human consumption in confined areas used for HBOT are regularly monitored for purity (+/- 1%) and flow (10 to 15 liters per minute outflow pressure). An audible alarm will sound if the purity ever drops below 80%. Personal hyperbaric chambers use 120 volt or 220 volt outlets. Ranging in size from 21 inches up to 40 inches in diameter these chambers measure between 84 in (7 ft) to 120 in (10 ft) in length. The soft chambers are approved by the FDA for the treatment of altitude sickness, but are commonly used for other “off-label” purposes.

**Possible complications and concerns**

There are risks associated with HBOT, similar to some diving disorders. Pressure changes can cause a “squeeze” or barotrauma in the tissues surrounding trapped air inside the body, such as the lungs, behind the eardrum, inside paranasal sinuses, or trapped underneath dental fillings. Breathing high-pressure oxygen may cause oxygen toxicity. Temporarily blurred vision can be caused by swelling of the lens, which usually resolves in two to four weeks.

There are reports that cataract may progress following HBOT. Also a rare side effect has been blindness secondary to optic neuritis (inflammation of the optic nerve).
Effects of pressure

Patients inside the chamber may notice discomfort inside their ears as a pressure difference develops between their middle ear and the chamber atmosphere. This can be relieved by ear clearing using the Valsalva maneuver or other techniques. Continued increase of pressure without equalising may cause ear drums to rupture, resulting in severe pain. As the pressure in the chamber increases further, the air may become warm.

To reduce the pressure, a valve is opened to allow air out of the chamber. As the pressure falls, the patient’s ears may “squeak” as the pressure inside the ear equalizes with the chamber. The temperature in the chamber will fall. The speed of pressurization and de-pressurization can be adjusted to each patient’s needs.

Costs

HBOT is recognized by Medicare in the United States as a reimbursable treatment for 14 UHMS “approved” conditions. A 1-hour HBOT session may cost between $165 and $250 in private clinics, and over $2,000 in hospitals. U.S. physicians (either M.D., D.O., D.D.S., D.M.D., D.C.) may lawfully prescribe HBOT for “off-label” conditions such as stroke, and migraine. Such patients are treated in outpatient clinics. In the United Kingdom most chambers are financed by the National Health Service, although some, such as those run by Multiple Sclerosis Therapy Centres, are non-profit. In Australia, HBOT is not covered by Medicare as a treatment for multiple sclerosis. The average U.S. hospital charge is $1,800.00 per 90 minute HBOT treatment. China and Russia treat more than 80 maladies, conditions and trauma with HBOT.

Research

The University of Birmingham’s 2012 guidance to West Midlands primary care trusts and clinical commissioning groups concluded “The primary research studies investigating the efficacy of HBO are remarkable for the consistent poor quality of the published clinical trials as well as the lack of evidence
demonstrating significant health benefits. There is a lack of adequate clinical evidence to support the view that HBO therapy is efficacious for any of the indications for which it is being used”.

Aspects under research include radiation-induced hemorrhagic cystitis; and inflammatory bowel disease.

**Neurological**

Tentative evidence shows a possible benefit in cerebrovascular diseases. The clinical experience and results so far published has promoted the use of HBO therapy in patients with cerebrovascular injury and focal cerebrovascular injuries. However, the power of clinical research is limited because of the shortage of randomized controlled trials.

**Radiation wounds**

A 2010 review of studies of HBOT applied to wounds from radiation therapy reported that, while most studies suggest a beneficial effect, more experimental and clinical research is needed to validate its clinical use.

**HISTORY**

**Hyperbaric air**

The use of air at raised ambient pressure for the treatment of illness is recorded from 1662 for afflictions of the lung, by Henshaw. It is unlikely to have had any significant effect.

Junod built a chamber in France in 1834 to treat pulmonary conditions at pressures between 2 and 4 atmospheres absolute.

During the following century “pneumatic centres” were established in Europe and the USA which used hyperbaric air to treat a variety of conditions.

Orval J Cunningham, a professor of anaesthesia at the University of Kansas in the early 1900s observed that people suffering from circulatory disorders did better at sea level than at altitude and this formed the basis for his use of hyperbaric air.
In 1918 he successfully treated patients suffering from the Spanish flu with hyperbaric air. In 1930 the American Medical Association forced him to stop hyperbaric treatment, since he did not provide acceptable evidence that the treatments were effective.

**Hyperbaric oxygen**

The English scientist Joseph Priestley discovered oxygen in 1775. Shortly after its discovery, there were reports of toxic effects of hyperbaric oxygen on the central nervous system and lungs, which delayed therapeutic applications until 1937, when Behrke and Shaw first used it in the treatment of decompression sickness.

In 1955 and 1956 Churchill-Davidson, in the UK, used hyperbaric oxygen to enhance the radiosensitivity of tumours, while Ite Boerema, at the University of Amsterdam, successfully used it in cardiac surgery.

In 1961 WH Brummelkamp et al. published on the use of hyperbaric oxygen in the treatment of clostridial gas gangrene.

In 1962 Smith and Sharp reported successful treatment of carbon monoxide poisoning with hyperbaric oxygen.

The Undersea Medical Society (now Undersea and Hyperbaric Medical Society) formed a Committee on Hyperbaric Oxygenation which has become recognized as the authority on indications for hyperbaric oxygen treatment.

**USE OF OXYGEN THERAPY IN COPD**

PatientPlus articles are written by UK doctors and are based on research evidence, UK and European Guidelines. They are designed for health professionals to use, so you may find the language more technical than the condition leaflets.

**GENERAL POINTS ABOUT OXYGEN THERAPY IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE**

- There is strong evidence of survival benefit of long-term oxygen therapy (LTOT) in patients with COPD and
severe chronic hypoxaemia when used for at least 15 hours daily.

- Therefore, oxygen therapy in COPD must be used with care in the acute setting but it can have distinct benefits in the long term. Chronic hypoxaemia causes slowly progressive pulmonary hypertension with the development of right ventricular hypertrophy and possible cor pulmonale with secondary polycythaemia. Secondary polycythaemia increases blood viscosity and hence resistance to flow. There is also sludging and a tendency to thrombosis.

- A Cochrane review of randomised controlled trials (RCTs) of domiciliary oxygen therapy for COPD found:
  - Long-term home oxygen therapy improved survival in a selected group of COPD patients with severe hypoxaemia (arterial PaO_2 less than 55 mm Hg (8.0 kPa)).
  - Home oxygen therapy did not appear to improve survival in patients with mild-to-moderate hypoxaemia or in those with only arterial desaturation at night.

- National Institute for Health and Care Excellence Clinical Knowledge Summaries recommend that, if the patient will not stop smoking, oxygen therapy should be withheld. There is a real risk of fire and burns to the face and any benefit relating to polycythaemia is counteracted by smoking.

**Oxygen therapy in the acute setting (in hospital)**

- For most COPD patients, you should be aiming for an SaO_2 of 88-92%, (compared with 94-98% for most acutely ill patients NOT at risk of hypercapnic respiratory failure). Mark the target saturation clearly on the drug chart.

- The aim of (controlled) oxygen therapy is to raise the PaO_2 without worsening the acidosis. Therefore, give oxygen at no more than 28% (via venturi mask, 4 L/minute) or no more than 2 L/minute (via nasal prongs) and aim for
Oxygen supplementation, delivery and physiologic effects

Oxygen saturation 88-92% for patients with a history of COPD until arterial blood gases (ABGs) have been checked.
• Treat patients aged over 50 with possible COPD in the same way (eg, long-term smokers with a history of chronic breathlessness) and get ABGs urgently.

It is particularly important to check ABGs promptly if the patient has been brought in as emergency by an ambulance: ambulance crews have to give high-flow oxygen if a patient is hypoxic, regardless of previous history.
• Measure ABGs within 60 minutes of starting supplemental oxygen or changing its concentration. If PaO₂ improves with an associated drop in PaCO₂ and the pH is relatively unaffected (pH >7.26) then the concentration of the supplemental oxygen may be increased to maintain PaO₂ >7.5 kPa.
• Oxygen therapy will have to be complemented with other interventions for any acute exacerbation of COPD.
• If acidosis develops (falling pH) with a rising PaCO₂, other therapeutic interventions need to be discussed with the acute medical team; the intensive treatment unit (ITU) may need to be involved and decisions regarding ceiling of care have to take place at this point. Non-invasive positive pressure ventilation (NIPPV), intermittent positive pressure ventilation (IPPV) and doxapram are all options.
• Check ABGs on air before discharge in those who presented with a low pO₂ and/or hypercapnia to guide later formal assessment for LTOT.
• 4- to 6-week follow-up should include consideration of LTOT assessment - not before, as the patient needs to be clinically stable.

Long-term oxygen therapy

Once this is started, LTOT is likely to be lifelong. It is usually given over a minimum of 15 hours a day, including overnight
when arterial hypoxaemia worsens during sleep (some advocate 18 or even 24 hours a day).

• Assess the need for oxygen therapy in people with any of the following:
  o Very severe airflow obstruction - forced expiratory volume in one second (FEV₁) less than 30% predicted.
  o Cyanosis.
  o Polycythaemia.
  o Peripheral oedema.
  o Raised jugular venous pressure.
  o Oxygen saturation 92% or below when breathing air.
• Consider assessment for people with severe airflow obstruction (FEV₁ 30-49% predicted).
• Assess by measuring ABGs on two occasions at least three weeks apart in people with confirmed stable COPD who are receiving optimum medical management. Obtaining ABGs in the community can be difficult and may require a visit to the local hospital or involvement of the specialist respiratory nurse.
• Offer LTOT to people with PaO₂ less than 7.3 kPa when stable (or less than 8 kPa when stable and with peripheral oedema, polycythaemia (haematocrit e55%) or pulmonary hypertension).
• Be aware that inappropriate oxygen therapy in people with COPD may cause respiratory depression.
• All healthcare settings should have a pulse oximeter to ensure all people needing LTOT are identified and to review people receiving LTOT at least once a year.
• People receiving LTOT should breathe supplemental oxygen for at least 15 hours a day. If they smoke, warn them about the risk of fire and explosion.
• Use oxygen concentrators to provide the fixed supply for LTOT at home.
Oxygen Supplementation, Delivery and Physiologic Effects

• Refer people who are hypercapnic or acidotic on LTOT to a specialist centre for consideration of long-term non-invasive ventilation (NIV).

• NIV should be used as the treatment of choice for persistent hypercapnic ventilatory failure during exacerbations not responding to medical therapy.

Ambulatory oxygen therapy

• Offer ambulatory oxygen therapy (AOT) to people already on LTOT who want to use oxygen outside the home, following assessment by a specialist.

• Consider it in motivated individuals who have exercise desaturation and PaO$_2$ less than or equal to 7.3 kPa and whose exercise capacity and/or breathlessness improve with oxygen.

The British Thoracic Society (BTS) recommends:

• AOT should not be routinely offered to patients who are not eligible for LTOT.

• AOT should not be routinely offered to patients already on LTOT.

• AOT assessment should only be offered to patients already on LTOT if they are mobile outdoors.

• AOT should be offered to patients for use during exercise in a pulmonary rehabilitation programme or during an exercise programme following a formal assessment demonstrating improvement in exercise endurance.

Short-burst oxygen therapy

• Short-burst oxygen therapy (SBOT) is typically given to patients for the relief of breathlessness not relieved by any other treatments.

• It is used intermittently at home for short periods - for example, 10-20 minutes at a time.
• Oxygen used in this way has traditionally been ordered for non-hypoxaemic patients and used for subjective relief of dyspnoea prior to exercise for oxygenation or after exercise for relief of dyspnoea and recovery from exertion.

• Consider SBOT (from cylinders) only for episodes of severe breathlessness not relieved by other treatments and continue only if breathlessness improves.

Prescription

Prescribing Oxygen for full details but some aspects are repeated here.

• Patients need to be assessed first by a specialist team before a GP can make the prescription.

• The supply of home oxygen has been transferred from community pharmacies to regional oxygen supply companies. These companies are responsible for supplying cylinders, concentrators and liquid oxygen as part of an integrated service.

• Oxygen should be ordered directly from one of four regional supply companies via the Home Oxygen Order Form (HOOF). This has replaced prescribing of oxygen on FP10 prescriptions.

• Form completion notes are on the back - ensure you specify all the details (notably, the oxygen concentration).

• Regular orders should take three days; emergency ones should be delivered in four hours.

• The NHS home oxygen service is available throughout the UK. However, delivery is different in Scotland and Northern Ireland:
  o In Scotland patients should be referred for assessment by a respiratory consultant. If the need for a concentrator is confirmed the consultant will arrange for the provision of a concentrator through the Common Services Agency.
  o In Northern Ireland oxygen concentrators and cylinders
Oxygen Supplementation, Delivery and Physiologic Effects

should be prescribed on form HS21. Oxygen concentrators are supplied by a local contractor.
• In Scotland and Northern Ireland prescriptions for oxygen cylinders and accessories can be dispensed by pharmacists contracted to provide domiciliary oxygen services.

Maximising benefit
• As a general rule, it is more economical to use an oxygen concentrator rather than cylinders if oxygen is required for more than eight hours per day or if prescriptions exceed 21 cylinders per month. Use nasal prongs at 2-4 L/minute (depending on ABGs).
• There is no benefit from LTOT for less than 15 hours a day.
• Smokers should stop smoking or benefit is unlikely. There is a very significant risk of burns and fire.
• Get optimum benefit from other forms of therapy, including inhalers.

Monitoring
• The patient’s ABGs need to be monitored. Simply measuring $\text{SaO}_2$ is not enough, as assessment of hypercapnia and its response to oxygen therapy is required.
• ABGs can be radial, femoral or from the earlobe. Collect a sample when the patient has been breathing air for at least 30 minutes after having received any prior supplemental oxygen.
• Once therapy has started, measure ABGs with oxygen therapy (for at least 30 minutes on therapy, using the same equipment as at home if possible), to assess response and ensure $pO_2$ is $>8.0$ kPa without unacceptable hypercapnia.
• Subsequently, measure ABGs when the patient is clinically stable and on optimal therapy on two occasions at least three weeks apart.
• All patients should be visited at home within four weeks of prescription by a specialist nurse, physiotherapist or
technician (depending on local arrangements), experienced in the provision of domiciliary oxygen therapy. The aim is to provide education and support and to measure the $\text{SaO}_2$ with oximetry both on air and with therapy. This should be 92% or above with therapy.

- It is important to maintain six-monthly follow-up with reassessment for early recognition of problems. The BTS recommends domiciliary assessment by a respiratory health worker.

Travel

Travel by land or sea presents a few potential problems:

- Reduced $\text{pO}_2$ in airline cabins will increase hypoxia in those patients with hypoxia at sea level.
- The BTS states that commercial air travel is contra-indicated for patients with usual oxygen requirement at sea level at a flow rate exceeding 4 L/minute.
- Most major airlines can provide supplemental inflight oxygen and assistance with embarkation if arranged in advance.
- It is usually possible to arrange temporary provision of LTOT from a local chemist during a holiday but many patients can manage well without LTOT for several days.

SHORT-TERM EFFECTS OF OXYGEN ADMINISTRATION

In addition to relieving arterial hypoxemia and alleviation of the consequences listed above, supplemental oxygen has several therapeutic benefits. Oxygen improves breathlessness in both normal subjects and in those with COPD during exercise. Exercise tolerance is improved in those who develop significant hypoxemia as well as in those with only mild to moderate hypoxemia. Although this phenomenon has been observed by many investigators, the responsible mechanisms remain a matter of debate. In COPD, the perceived decrease in breathlessness and improvement in exercise
capacity may be due to decreased Ve, a decrease in dynamic hyperinflation, alleviation of hypoxic pulmonary vasoconstriction and improved hemodynamics (e.g., decrease in pulmonary vascular resistance and increase in cardiac output), or increased oxygen delivery. O’Donnell and colleagues performed cardiopulmonary exercise tests in 11 hypoxic and hypercapnic patients with severe COPD (\(\text{Pa}_{\text{O}_2}\) 52 ± 2 mm Hg, and \(\text{Pa}_{\text{CO}_2}\) 48 ± 2 mm Hg, respectively) while breathing room air or 60% \(\text{Fi}_{\text{O}_2}\) in random order. Oxygen administration resulted in a decrease in dyspnea scores, higher inspiratory capacity, and decreased respiratory rate compared with room air. Dean and coworkers randomized 12 patients with severe COPD to compressed air or 40% inhaled oxygen during exercise. In those treated with oxygen, cycle ergometry endurance time increased by 40%, maximal right ventricular systolic pressures (via Doppler echocardiography) decreased, and the rate of rise of right ventricular systolic pressure was decreased. Morrison and Stovall found that hypoxemic patients with COPD who showed an improvement in exercise capacity with supplemental oxygen had significant increases in both cardiac output and oxygen content during exercise.

Alternative proposed mechanisms include an improvement in ventilatory muscle function and altered ventilatory muscle recruitment. Oxygen flow may also stimulate upper airway and facial receptors of the trigeminal nerve and reflexively inhibit central ventilatory drive. Finally, there also appears to be a direct effect of oxygen administration on the perception of dyspnea independent of any changes in Ve. On the basis of these studies, it has been recommended by some to use supplemental oxygen for all patients with COPD while undergoing pulmonary rehabilitation. However, the current evidence does not support the routine use of oxygen in normoxemic patients with COPD during exercise.

Oxygen administration decreases Ve and work of breathing during acute respiratory failure (ARF) in COPD. A study conducted in 20 patients with COPD, both in a chronic stable condition and
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during ARF, found no difference in Ve between patients with chronic, stable COPD and normal control subjects. In ARF, however, application of oxygen at 5 L/minute decreased Ve by 14%, mostly by a decrease in respiratory rate without a compensatory increase in tidal volume. ARF was also associated with increased work of breathing, as evidenced by a fivefold increase in mouth occlusion pressure. This rise in mouth occlusion pressure decreased by 40% after oxygen administration. These effects of oxygen on ventilation and work of breathing may help prevent respiratory muscle fatigue during ARF, particularly in patients with chronic respiratory insufficiency who have a higher baseline ventilatory demand.

Effect Of Ltot On Mortality

Chronic hypoxemia leading to the development of cor pulmonale portends a poor prognosis, with mortality ranging anywhere from 32 to 100%. Early noncontrolled studies showed a reduction in mortality in patients with COPD, cor pulmonale, and severe hypoxemia with the use of continuous oxygen therapy for 7 to 41 months. Two landmark studies performed in the late 1970s, the Nocturnal Oxygen Therapy Trial (NOTT) and the British Medical Research Council (MRC) Long-Term Domiciliary Oxygen Therapy Trial, examined the effects of LTOT on survival and physiologic function in patients with severe chronic bronchitis and emphysema.

The British MRC trial was conducted in the late 1970s and reported in March of 1981. It was performed in three centers in the United Kingdom and enrolled 87 patients, all younger than 70 years, who had chronic bronchitis or emphysema with irreversible airway obstruction (FEV₁ range, 0.58–0.75 L), severe hypoxemia (P_{aO₂} range, 49.4–51.8 mm Hg), carbon dioxide retention (P_{aCO₂} 56–60 mm Hg), and a history of cor pulmonale (mean pulmonary artery pressure range, 32.3–35.0 mm Hg). Patients randomized to receive oxygen were given 2 L/minute of oxygen via nasal prongs for at least 15 hours a day. In 5 years of survival follow-up, 19 of the 42 oxygen-treated patients died, compared
with 30 of 45 control subjects who did not receive oxygen and died. Mortality appeared to be highest in the subgroup of patients who had the highest elevations in baseline $\text{Pa}_{\text{CO}_2}$ and red cell mass. Although mortality was favorably affected by long-term oxygen use, there were no statistically significant differences in the rate of decrease of $\text{FEV}_1$, or $\text{Pa}_{\text{A}t}$, or increase in $\text{Pa}_{\text{CO}_2}$, red cell mass, or pulmonary artery pressures. However, there appeared to be a trend that LTOT prevented a progressive decrease in $\text{Pa}_{\text{A}t}$ and in the rate of increase in pulmonary vascular resistance without provoking a further increase in $\text{Pa}_{\text{CO}_2}$.

The NOTT, sponsored by the National Heart, Lung, and Blood Institute, reported the effects of continuous versus nocturnal oxygen therapy in hypoxemic patients with COPD. This multicenter study enrolled 203 hypoxemic patients with COPD who were randomly allocated to receive either continuous oxygen therapy or 12 hours of nocturnal oxygen therapy. All subjects were followed for at least 12 months to determine the effects of oxygen therapy on survival, pulmonary vascular pressures, neuropsychological function, and quality of life. Mortality in the 203 patients was followed for an average of 19.3 months. Eighty nocturnal oxygen and 87 continuous oxygen therapy subjects were followed for 12 months, whereas 29 nocturnal oxygen and 37 continuous oxygen therapy patients were followed for 24 months. Overall mortality of the subjects assigned to continuous oxygen therapy and nocturnal oxygen therapy over 3 years of observation. A total of 64 subjects died in the trial, 41 in the nocturnal oxygen therapy group and 23 in the continuous oxygen therapy group. At all six centers, mortality for the nocturnal oxygen therapy group exceeded that for the continuous oxygen therapy group.

When the effect of continuous versus nocturnal therapy was assessed for its impact on physiologic variables, no significant changes were found in arterial blood gas values, lung volumes, $\text{FEV}_1$, maximum work attained, mean pulmonary artery pressures, or cardiac index. However, hematocrit values were more reduced in patients on continuous oxygen therapy than those randomized
to nocturnal treatment (<7% difference), as was pulmonary vascular resistance (17.6% greater decrease in pulmonary vascular resistance found in the group receiving continuous vs. nocturnal therapy).

It should be recognized that, although both of the above studies showed improved survival, patients were not comparable between studies. Patients in the MRC study tended to be more ill and with more evidence of resting hypercapnia and cor pulmonale. Furthermore, patients in the MRC study had a significant number of participants who continued to smoke even after enrollment into the trial (27% in the control group and 44% in the placebo group), whereas no comment was made on the incidence of continued smoking in NOTT patients.

Finally, the MRC study found no statistically significant impact of nocturnal oxygen therapy versus no oxygen treatment on physiologic variables, whereas the NOTT study found a statistically significantly greater decrease in pulmonary vascular resistance and absolute hematocrit associated with continuous oxygen therapy. The causal relationship between a reduction in hematocrit and pulmonary vascular resistance on influencing survival, whether using continuous or nocturnal oxygen therapy, was not established, however.

Despite their differences, these two prospective and controlled trials appear to establish that nocturnal oxygen therapy is better than no oxygen therapy at all, and continuous oxygen therapy is better than nocturnal oxygen therapy in severely hypoxemic patients with elevated hematocrit, pulmonary artery pressure, and respiratory acidosis. In an attempt to extend the above findings to patients who suffer from less severe disease and only moderate hypoxemia, Gorecka and colleagues evaluated 135 patients (PaO₂ 56–65 mm Hg at rest) with advanced airflow obstruction (FEV₁, 0.83 L) who were randomly allocated to receive no oxygen therapy or LTOT. Patients assigned to either group were followed every 3 months for at least 3 years. The cumulative survival rates for the group at large were 88% at 1 year, 77% at 2 years, and 66%
at 3 years. The authors found no significant difference in survival rates between the two patient groups treated with LTOT versus control therapy. Patients who were younger, had better spirometric values, and had higher body mass index showed better survival. This was similar to the findings of other studies, in which no survival benefit was found in patients with COPD given supplemental oxygen when severe hypoxemia or cor pulmonale was not present.

Similarly, no study has shown a survival benefit when oxygen is prescribed for exercise-induced oxygen desaturation. Most recently, the National Emphysema Treatment Trial (NETT) research group performed a retrospective analysis on the normoxemic participants in the medical arm of NETT (unpublished data). They found that the normoxemic patients who reported continuous oxygen use had greater dyspnea, lower quality of life, worse lung function, worse exercise capacity, and more frequent exercise desaturation compared with the normoxemic patients who did not use oxygen therapy. In those who experienced desaturation during exercise, no difference in survival was found based on reported oxygen use. It must be noted, however, that oxygen use was not given in a prospective, randomized fashion, and the available data may help identify a sicker group of patients with a greater risk of death.

**Oxygen Therapy And Pulmonary Hemodynamics In COPD**

Substantial evidence suggests that the presence of secondary pulmonary hypertension in COPD increases the risk for hospitalization and is associated with worsened survival. Because of the known association of resting hypoxemia with the development of secondary pulmonary hypertension, investigators have focused on supplemental oxygen as treatment for hypoxemic COPD patients with pulmonary hypertension. Data from the NOTT group found that oxygen therapy in hypoxemic patients with COPD is associated with favorable but minimal changes in the magnitude of pulmonary hypertension at rest and during exercise.
Furthermore, they tend to suggest that favorable changes in pulmonary hemodynamics secondary to oxygen supplementation are enhanced in the group of patients that receives oxygen continuously, compared with those who receive it on an intermittent daily basis. It is difficult to attribute the improvements in survival of patients with COPD receiving continuous versus nocturnal oxygen therapy solely to changes in pulmonary hemodynamics on the basis of the available data. In addition, the response to acute administration of oxygen on pulmonary hemodynamics does not appear to predict the long-term effects of oxygen therapy on survival. Further studies are required to determine the causal relationship of oxygen supplementation on pulmonary hemodynamics and survival, and to predict which subgroups of patients with pulmonary hypertension and hypoxemic COPD are more likely to benefit from long-term administration.

**Oxygenation And Sleep In COPD**

Sleep disturbance is common in patients with COPD. Increased sleep latency, decreased total sleep time, decreased slow-wave sleep, and decreased REM sleep have been noted in many polysomnographic studies of patients with COPD. Approximately 30 to 70% of patients with COPD complain of insomnia, early morning awakenings, morning tiredness, or daytime sleepiness. Common reasons include medication side effects, airflow obstruction, and hypercapnia, but perhaps the most important is nocturnal oxygen desaturation (NOD). Approximately 25 years ago, Koo and colleagues studied 15 normoxemic patients with severe COPD (FEV₁, 0.96 L) and found a mean decrease in PaO₂ of 13.5 mm Hg and a mean increase of PaCO₂ of 8.3 mm Hg during REM sleep. Up to 25% of patients with COPD exhibit REM-related hypoventilation and NOD, despite having a daytime PaO₂ above 60 mm Hg. Determining who will develop NOD is difficult without nocturnal oximetry or polysomnography; assessments of daytime gas exchange or pulmonary function are unable to differentiate those patients who experience desaturation at night and those who do not. It has been suggested that oxygen therapy improves
sleep continuity and quality in those who experience desaturation, although this phenomenon has not been demonstrated in all studies.

NOD may lead to the development of pulmonary hypertension and cor pulmonale in patients with COPD. Levi-Valensi and coworkers investigated the relationship between sleep variables and daytime pulmonary hemodynamics in 40 patients with COPD with daytime Pa\textsubscript{O2} of 60 to 70 mm Hg. Mean pulmonary artery pressure was higher in those who demonstrated significant oxygen desaturation compared with those who did not (19.1 ± 4.7 vs. 16.9 ± 1.9 mm Hg, respectively). Oxygen therapy during sleep may prevent nocturnal hypoxemia and possibly the development of pulmonary hypertension. However, two recent clinical studies examining normoxemic patients with COPD with evidence of nocturnal desaturation found neither an improvement in survival with nocturnal oxygen despite a reduction in pulmonary artery pressures nor a delay in the time to prescription of continuous oxygen therapy. Therefore, similar to exercise-induced hypoxemia, it is unclear whether LTOT in this circumstance has long-term benefits. Given the lack of survival advantage, screening for nocturnal desaturation in normoxemic patients with COPD should probably be reserved for those with hypercapnia, erythrocytosis, or evidence of pulmonary hypertension.

**Oxygen And Air Travel**

Ascent to high altitude via air travel exposes patients to hypobaric conditions, which increases risk of hypoxemia. Pressurizing the aircraft cabin limits the fall in atmospheric pressure to an altitude of 8,000 ft, allowing ascent to much higher altitudes. Oxygen supplementation is indicated if the predicted Pa\textsubscript{O2} at 8,000 ft is less than 50 mm Hg. Those with an Sp\textsubscript{O2} greater than 95% or a Pa\textsubscript{O2} greater than 72 mm Hg while breathing ambient air at sea level will most likely not require oxygen supplementation. For those who do not meet these criteria, an equation has been advocated to predict Pa\textsubscript{O2} at an 8,000-ft altitude in normocapnic patients with COPD:
\[ \text{Pa}_\text{O}_2 \text{ at 8.00 ft} = [0.235 \times (\text{Pa}_\text{O}_2 \text{ sea level})] + [20.098 \times (\text{FEV1}/\text{FVC})] + 22.258 \]

Determining the liter flow needed to restore normoxemia during flight is slightly more difficult. In one series, the use of 2 L/minute of supplemental oxygen was sufficient for those who did not require oxygen at sea level.

Predicting the liter flow for those who already require oxygen at sea level can be done with a hypoxic gas inhalation test. Using a 35% Venturi mask with nitrogen as the supply gas instead of oxygen, the entrained ambient air will result in a fraction of inspired oxygen of 16%, thereby mimicking the hypoxic conditions at approximately 6,700 ft. The \( \text{Pa}_\text{O}_2 \) can be measured while the patient is breathing in supplemental oxygen through a nasal cannula.
Nasal CPAP: An Evidence-Based Assessment

NASAL CPAP

CPAP stands for continuous positive airway pressure. CPAP pumps air under pressure into the airway of the lungs, keeping the windpipe open during sleep. The forced air delivered by CPAP prevents episodes of airway collapse that block the breathing in people with obstructive sleep apnea and other breathing problems.

It is sometimes called nasal continuous positive airflow pressure (nCPAP).

Information

Who Should Use CPAP

CPAP can successfully treat most people with obstructive sleep apnea. It is safe and works well for people of all ages, including children. If you only have mild sleep apnea and do not feel very sleepy during the day, you may not need it.

After using CPAP regularly, you may notice:

• Better concentration and memory
• Feeling more alert and less sleepy during the day
• Improved sleep for your bed partner
• Being more productive at work
• Less anxiety and depression and a better mood
• Normal sleep patterns
• Lower blood pressure (in people with high blood pressure)

CPAP works by keeping a steady pressure of forced air in your airway to keep it open. Other devices work in slightly different ways to treat sleep apnea:

• Autotitrating positive airway pressure (APAP) changes pressure throughout the night based on your breathing patterns.
• Bilevel positive airway pressure (BiPAP) has a higher pressure when you breathe in and lower pressure when you breathe out.

BiPAP is useful for children and adults who have:
• Airways that collapse while sleeping, making it hard to breathe freely
• Decreased air exchange in the lung
• Muscle weakness that makes it difficult to breathe, due to conditions such as muscular dystrophy

CPAP or BiPAP may also be used by people who have:
• Respiratory failure
• Central sleep apnea
• COPD
• Heart failure

**How CPAP Works**

When using CPAP:
• You wear a mask over your nose or nose and mouth while you sleep.
• The mask is connected by a hose to a small machine that sits at the side of your bed.
• The machine pumps air under pressure through the hose and mask and into your airway while you sleep. This helps keep your airway open.

You may start to use CPAP while you are in the sleep center for the night.
• Your health care provider will help choose the mask that fits you best.
• They will adjust the settings on the machine while you are asleep.
• The settings will be adjusted based on the severity of your sleep apnea.

If you are using CPAP but your symptoms do not improve, the settings on the machine may need to be changed. Your provider may teach you how to adjust the CPAP at home. Or, you may need to go to the sleep center to have it adjusted.

**Getting Used To The Device**

It can take time to get used to using a CPAP device. The first few nights of CPAP therapy are often the hardest. You may not sleep well at the start of treatment.

If you are having problems, you may be tempted not to use CPAP for the whole night. But, you will get used to it more quickly if you use the machine for the entire night.

When using CPAP for the first time, you may have:
• A feeling of being closed in (claustrophobia)
• Chest muscle discomfort, which usually goes away after awhile
• Eye irritation
• Redness and sores over the bridge of your nose
• Runny or stuffed-up nose
• Sore or dry mouth
• Nosebleeds
• Upper respiratory infections
Many of these problems can be helped or prevented.

- Ask your doctor or therapist about using a mask that is lightweight and cushioned. Some masks are used only around or inside the nostrils.
- Make sure the mask fits correctly so that it does not leak air. It should not be too tight or too loose.
- Try nasal salt water sprays for a stuffed nose.
- Use a humidifier to help with dry skin or nasal passages.
- Keep your CPAP equipment clean.
- Place your CPAP machine underneath your bed to limit noise.
- Most machines are quiet, but if you notice sounds that make it hard to sleep, tell your doctor or therapist.

Your doctor or therapist can lower the pressure on the CPAP machine and then increase it again at a slow pace. Some new machines can automatically adjust to the pressure that is needed.

**WHAT IS NASAL CPAP THERAPY?**

Nasal continuous positive airway pressure (CPAP) therapy is a nonsurgical treatment that provides a steady flow of air to the lungs through the nose. Nasal CPAP is a common treatment for those with obstructive sleep apnea, a sleep disorder that disrupts normal breathing and interrupts deep sleep. It may also help infants with underdeveloped lungs breathe more easily.

**Who Needs Nasal CPAP Therapy?**

Individuals of all ages who have obstructive sleep apnea often make good candidates for nasal CPAP therapy. Sleep apnea is a chronic condition that disrupts sleep. Frequent pauses in breathing actually stop the flow of air to the lungs. After each pause, the body’s natural defenses kick in to start the breathing again, pulling the individual out of the deep sleep stage.

Some obstruction in the airway typically creates these pauses in breath. Throat muscles that relax too much to allow normal
breathing can block the flow of air. A large tongue or tonsils may also create an obstruction. A blocked airway can cause the individual to snort, choke, or gasp. At this point, the problem tends to correct itself and breathing resumes, only to become blocked again moments later.

**What Are the Symptoms of Sleep Apnea?**

The corrective periods in between pauses are often so brief that the individual doesn’t remember them. That’s why in many cases, sleep apnea goes undetected. Symptoms, however, may include:

- snoring loudly (though not everyone who snores has sleep apnea)
- gasping or choking during sleep
- feeling irritable, depressed, grumpy, or impatient during the day
- falling asleep at the drop of a hat, such as while watching television, reading, or even working
- forgetting things
- having frequent or hard-to-treat headaches
- having morning dry mouth or sore throat

Though sleep apnea may seem at most an irritation, the disorder can be life-threatening. Without treatment, sleep apnea can increase the risk of:

- heart attack
- stroke
- irregular heartbeat
- high blood pressure
- other related conditions

Fortunately, treatment is most always successful at reducing these risks and restoring sound sleep.

**What Is a Nasal CPAP Device?**

People with mild sleep apnea may find relief through simple
Pediatric and Neonatal Mechanical Ventilation

lifestyle changes, such as avoiding alcohol, losing weight, and using nasal sprays or allergy medications. Others breathe more easily with a custom-made mouthpiece or oral appliance that adjusts the position of the lower jaw and tongue to help keep airways open during sleep.

Individuals with moderate to severe obstructive sleep apnea, however, often require a breathing device called a nasal CPAP machine.

This device blows air into your nose through a nose mask, helping to keep the airway open while you sleep.

A small machine, called an air compressor, is placed on a bedside table and connected to a tube and mask that fits over your nose.

This machine delivers a steady flow of air through the tube and mask, exerting just enough pressure to keep muscles and tissues from collapsing and blocking the airway.

Your doctor or nurse will help you choose the mask that best fits over your nose, and then will adjust the settings on the CPAP machine to the pressure required for your condition. If you don’t notice improvements after a week or so, check back with your doctor, as they may need to adjust the pressure settings.

After using the machine regularly, most patients report dramatic benefits, including the following:

- improved sleep
- less anxiety and better overall mood
- improved concentration and memory
- increased productivity

What Are the Complications Associated with Nasal CPAP Therapy?

Though most people get used to using the CPAP machine over time, others experience problems. These may include the following:
Runny Nose, Earache, or Sore Eyes

These may be due to an ill-fitting mask. An improved fitting can correct this. A heated humidifier attached to the machine may also help.

Sore or Inflamed Skin

This is also usually the result of an ill-fitting mask, or one that’s too heavy or improperly cushioned.

Claustrophobic Sensation of Feeling Closed-In

Different types of masks with straps that cover less of your face may help.

Uncomfortable Sensations with Forced Air

The “ramp” feature on the machine allows you to start with lower air pressure, which can help you better tolerate this sensation. If this doesn’t help, other machines (called BiPAPs) that automatically adjust pressure while you’re sleeping may help.

Dry Mouth

If this problem doesn’t go away after a few weeks, ask your doctor about a CPAP device that covers both your nose and mouth.

In most cases, working with your doctor to make adjustments to your device will result in a solution that will feel more comfortable.

CONTINUOUS POSITIVE AIRWAY PRESSURE

Continuous positive airway pressure (CPAP) is a form of positive airway pressure ventilator, which applies mild air pressure on a continuous basis to keep the airways continuously open in people who are able to breathe spontaneously on their own. It is an alternative to positive end-expiratory pressure (PEEP). Both modalities stent the lungs’ alveoli open and thus recruit more of the lung’s surface area for ventilation. But while PEEP refers to devices that impose positive pressure only at the end of the
exhalation, CPAP devices apply *continuous* positive airway pressure throughout the breathing cycle. Thus, the ventilator itself does not cycle during CPAP, no additional pressure above the level of CPAP is provided, and patients must initiate all of their breaths.

CPAP typically is used for people who have breathing problems, such as sleep apnea. CPAP also may be used to treat preterm infants whose lungs have not yet fully developed. For example, physicians may use CPAP in infants with respiratory distress syndrome.

It is associated with a decrease in the incidence of bronchopulmonary dysplasia. In some preterm infants whose lungs haven’t fully developed, CPAP improves survival and decreases the need for steroid treatment for their lungs.

CPAP therapy utilizes machines specifically designed to deliver a constant flow of pressure. Some CPAP machines have other features as well, such as heated humidifiers. CPAP is the most effective treatment for obstructive sleep apnea, in which the mild pressure from the CPAP prevents the airway from collapsing or becoming blocked.

Although delivery of CPAP through a nasal mask is the most common modality of treatment, other systems exist for interfacing with adults and children.

Nasal CPAP is frequently used in infants, though its use is controversial. Studies have shown nasal CPAP reduces ventilator time but an increased occurrence of pneumothorax was also prevalent. Oral masks and naso-oral masks are often used when nasal congestion or obstruction is an issue. Devices that combine nasal pressure with maxillary advancement devices (MAD) also exist.

**High flow therapy**

Humidified high flow nasal airway respiratory support is a method of delivering a high per-minute volume of respiratory gas via nasal cannula. The respiratory gas is heated to near body
Nasal cannulae usually used for oxygen delivery typically deliver 1–6 liters of oxygen per minute. The \( \text{FiO}_2 \) — the percentage of oxygen inhaled by the patient — usually ranges roughly from 24% to 35%, as 100% \( \text{O}_2 \) delivered from the cannula is diluted with air at about 21% oxygen.

Flow rates for delivery of oxygen using typical nasal cannulae are limited because medical oxygen is anhydrous, and when delivered from a pressurized source the gas cools as it expands with the drop to atmospheric pressure. Delivery of cold, dry gas is irritating to the respiratory mucosa, can cause drying and bleeding of the nasal mucosa, can trigger bronchospasm in asthmatics, and can increase metabolic demand by cooling the body. Thus oxygen delivery by nasal cannula is limited to less than 6 liters per minute.

Even with quiet breathing, the inspiratory flow rate at the nares of an adult usually exceeds 12 liters per minute, and can exceed 30 liters a minute for someone with mild respiratory distress. The typical upper limit for oxygen delivery via nasal cannula of six liters a minute does not meet the inspiratory flow rates of the average adult, and therefore the oxygen is diluted with room air during inspiration.

Prior to the advent of HFT, when high \( \text{FiO}_2 \) was required for respiratory support, special face masks or intubation were required. With HFT, respiratory gas flow volume is delivered which meets or exceeds the patient’s inspiratory flow rate, and is heated and humidified, allowing for comfortable delivery of respiratory support.

For HFT, a source of oxygen is usually blended with compressed air. Hospitals usually have 350 kPa (50 psi) compressed \( \text{O}_2 \) and air available for therapeutic use. This allows the delivery
of air, blends of air and O\textsubscript{2} from 22\% to 99\%, or delivery of 100\% oxygen with the use of an oxygen blender. The gas is then heated, generally to about 37 °C (98.6 °F), and humidified to near 100\% relative humidity using a humidifier. The gas is transported to the patient through a heated delivery tube to prevent cooling and condensation of the water vapor which has been added to the respiratory gas(es).

HFT requires the use of a special nasal cannula and tubing large enough to deliver flow rates of respiratory gas of up to 50 liters per minute in adults. At the same time, the nasal cannula must be small enough that it does not seal inside the nares, as this allows flow during exhalation and excess gas flow during inhalation to escape. If the cannula did seal, the high flow volume could produce excessive pressure in the airway and might provoke barotrauma.

Benefits

Since the delivered flow rate of HFT can meet the inspiration flow rate, the delivered gases are not diluted by room air. The FiO\textsubscript{2} is controlled by the clinician, and can be set from 21\% to 100\% oxygen. Nasal high flow therapy reduces respiratory dead space, and generates some positive airway pressure resulting from the expiratory resistance generated by continuous high-flow gas delivery. Flow rates exceeding inspiratory demand may also provide positive pressure during inspiration. Heated humidification of the respiratory gas facilitates secretion clearance and decreases the development of bronchial hyper-response symptoms. Some patients requiring respiratory support for bronchospasm benefit from using air delivered by HFT without additional oxygen. HFT is useful in the treatment of sleep apnea.

Neonates

Nasal HFT has shown to be useful in neonatal intensive care settings for premature infants with infant respiratory distress syndrome (RDS), as it prevents many infants from being intubated, and allows safe respiratory management at lower FiO2 levels, thus
reducing the risk of retinopathy of prematurity or other forms of oxygen toxicity.

**Settings and measurements**

- **CPAP:** This is the pressure applied without pause or end to the airway. Generally utilizing flow to generate the pressure.
- **PEEP:** Positive end-expiratory pressure (PEEP) is the pressure in the lungs (alveolar pressure) above atmospheric pressure (the pressure outside of the body) that exists at the end of expiration.
- **Ramp:** This feature is present on many devices and allows the user to reduce the pressure to lowest setting and gradually increase to the set pressure. This allows the user to fall asleep with the pressure at a more comfortable setting.
- **FIO2:** Fractional O2 percentage — that is, the fraction of inspired oxygen that is added to the delivered air.

**NASAL CPAP THERAPY**

Initially described in 1981, nasal CPAP therapy is the most effective treatment for OSA, and it has become the standard of care for this condition. (It is also effective for treating mixed apneas and some central apneas.)

The CPAP device consists of a blower unit that produces continuous positive-pressure airflow. This airflow is usually applied at the nose and is then directed through the UA. CPAP increases the caliber of the airway in the retropalatal and retroglossal regions. It increases the lateral dimensions of the UA and thins the lateral pharyngeal walls, which are thicker in patients with obstructive sleep apnea than in people without obstructive sleep apnea.

Top image is 3-dimensional surface renderings of the upper airway demonstrating the effect of progressive increases in
continuous positive airway pressure (CPAP) from 0-15 cm of water on upper-airway volume in a patient with upper airway narrowing. CPAP significantly increases airway volume in the retropalatal (RP) and retroglossal (RG) regions. Bottom image is soft tissue images in the same patient in the RP region at analogous levels of CPAP. With increasing CPAP, the upper airway progressively enlarges, particularly in the lateral dimension. Note the progressive thinning of the lateral pharyngeal walls as the level of CPAP increases. Little movement occurs in the parapharyngeal fat pads, the white structures lateral to the airway. The first image in each series depicts the baseline upper airway narrowing present in this patient.

Effectively, CPAP acts as a pneumatic splint to maintain UA patency during sleep, preventing the soft tissues from collapsing. By this mechanism, it effectively eliminates the apneas and/or hypopneas, decreases the arousals, and normalizes the oxygen saturation.

Effect of nasal continuous positive airway pressure (CPAP) on oxygen saturation in sleep apnea. The upper portion of this figure shows the raw oxygen saturation trace from 1 night of a sleep study. Below the raw trace are vertical lines that indicate the presence of either an apnea or hypopnea. Before CPAP, frequent respiratory events with significant desaturations occurred. During the night, CPAP was applied, resulting in the elimination of the apnea and hypopneas and normalization of the oxygen trace.

Guidelines for use

Patients with severe SDB (respiratory disturbance index [RDI] >20-30) should be treated irrespective of their symptoms because of the increased risk of cardiovascular morbidity. Patients with an RDI of 5-20 should be treated if they have symptoms or coexistent cardiovascular disease. Patients with UARS may need CPAP therapy.

Medicare guidelines specify criteria for ordering CPAP for patients with OSA. All patients with an apnea-hypopnea index
(AHI) greater than 15 are considered eligible for CPAP, regardless of symptomatology. For patients with an AHI of 5-14.9, CPAP is indicated only if the patient has one of the following: excessive daytime sleepiness (EDS), hypertension, or cardiovascular disease.

Most sleep center physicians still titrate CPAP during a sleep study, either as a second night of study or during the second half of a diagnostic study. Proper titration includes identifying the minimum CPAP level that abolishes obstructive apneas and/or hypopneas, oxyhemoglobin desaturation, respiratory effort-related arousals (RERAs), and snoring in all sleep stages and all sleep positions. The pressure needed is typically 5-20 cm H$_2$O. Guidelines for positive-pressure titration have been published. Currently, CPAP devices are available that automatically change pressures based on the presence and/or absence of OSA (auto–positive airway pressure, or auto-PAP). The rationale for auto-titrating devices is that the pressure required to treat OSA may vary over the course of the night and between different nights, sleep stages, and body positions, with the variations not captured by a one-night titration study.

In theory, the mean pressure delivered by auto-PAP devices is lower than that delivered with fixed CPAP; however, no studies have shown increased patient compliance with auto-PAP devices. In fact, a randomized crossover study comparing fixed and variable pressure CPAP, the largest to date (N = 200), found a marginal increase in hours used per night (0.2 h) but no difference in patient preference, which actually showed an order effect (patients preferred the type of device first used in the study). Guidelines from 2008 indicate that auto-PAP devices may be used during an attended sleep study to determine a single pressure for use at home (guideline recommendation). In addition, some evidence supports use in the unattended setting to determine a single pressure for home use (option recommendation).

Effectiveness

Application of adequate levels of nasal CPAP during sleep almost always resolves obstructive apnea and/or hypopnea, oxyhemoglobin desaturation, RERAs, and snoring from sleep. It
also results in adequate sleep continuity. CPAP has been shown to improve daytime sleepiness, mood, and cognitive function in people with both mild and moderate apnea. CPAP has also been shown to decrease blood pressure, primarily in patients with severe OSA. Evidence also indicates that it may improve the left ventricular ejection fraction in patients with congestive heart failure and OSA. CPAP plus an antihypertensive medication may synergistically improve systemic hypertension. In addition, it improves right-side heart function and pulmonary hypertension.

A study of 86 patients with sleep apnea, including 75 who had metabolic syndrome, suggests that CPAP is associated with a lower risk for heart disease, stroke, and diabetes. Study participants were treated for 3 months with either CPAP or sham CPAP, followed by a month of no treatment and 3 additional months of the opposite treatment. Of patients treated with CPAP, 13% no longer met diagnostic criteria for metabolic syndrome, compared with 1% of patients in the sham-CPAP control group. CPAP use was also associated with significant weight loss. CPAP has also been shown to increase quality of life and decrease health care costs. Prospective cohort studies suggest that CPAP reduces mortality in OSA. The benefits parallel those observed after tracheostomy.

Although many OSA patients note an immediate improvement in alertness, concentration, and memory, achieving maximum improvement in neurocognitive symptoms may take as long as 2 months. Follow-up visits should be scheduled at least once after CPAP treatment is first started and at least yearly thereafter. Follow-up evaluation is required to ensure symptomatic improvement, CPAP adherence, and equipment maintenance.

In an attempt to determine to what extent CPAP benefits its users, the authors of a randomized controlled trial evaluated the effects of stopping CPAP treatment. Results show a rapid recurrence of OSA and sleepiness within a few days of CPAP withdrawal. Also, study participants experienced deteriorated endothelial function and a marked increase in heart rate after 2
weeks. In one meta-analysis of three randomized placebo-controlled trials, nearly 30% of the treatment benefit among high users of CPAP was due to patients’ expected benefit of treatment due to their knowledge of hours of device use.

Adherence

CPAP adherence is key to patients obtaining benefits from its use. Unfortunately, adherence may be poor. Evidence indicates that many patients do not accept (or even initiate) CPAP therapy and that up to 25% do not regularly follow up with a sleep physician, with most of these patients being nonadherent to therapy.

Compliance with CPAP therapy can be objectively measured. Most modern CPAP devices measure both “machine-on” and “mask-on” times, with the mask-on time used to measure compliance. Compliance data are downloaded onto electronic chips from which compliance reports can be downloaded during follow-up appointments. These reports allow the physician to have real-time data on compliance, allowing him or her to immediately address problems. Examples of a compliance report are shown in the image below.

Examples of good (upper panel) and poor (lower panel) compliance. In the upper panel, the patient is using continuous positive airway pressure (CPAP) most nights and generally for more than 4 hours (solid black line). In the lower panel, the patient is using CPAP infrequently and, when used, is wearing the CPAP device for less than 4 hours.

Many studies have examined how many nightly hours use is necessary for CPAP to render salutary effects. A study published in 2009 demonstrated that persons who wore their CPAP device for 5.6 hours per night experienced a slight decrease in blood pressure. CPAP adherence was related to the AHI and decreased scores on the Epworth Sleepiness Scale (ESS); this effect was robust because patients with abnormal ESS scores were excluded from the study.

Generally, patients have been considered compliant if they use their CPAP device more than 4 hours per night, 5-7 nights per
week. However, a 2007 study questioned what is optimal CPAP usage. In this study, nightly duration of use required to normalize daytime functioning was examined for 3 common functional measures. The thresholds above which further improvements were less likely were 4 hours for the ESS score, 6 hours for the multiple sleep latency test (MSLT), and 7.5 hours for the Functional Outcomes of Sleep Questionnaire.

This study illustrates that patients who are considered to have good compliance by accepted definitions may, in fact, be undertreated and that patients should be encouraged to use positive airway pressure for at least 7 hours per night.

Evidence now indicates that CPAP compliance may be determined as early as 2 weeks after CPAP is initiated. Patients who consistently use their positive airway pressure device at 6 months were, on average, using the device for more than 2 hours more per night during the first 2 weeks and were more ready and confident to continue use. On the other hand, intermittent users were more likely to report adverse effects from the device, general discomfort, and that the device was too inconvenient.

In a study of long-term compliance, 68% of patients were using a CPAP machine at 5 years. Predictors of long-term compliance were baseline AHI and degree of sleepiness. However, the best predictor of compliance was regular use at 3 months of therapy, indicating that physicians must work to increase patient compliance early in the treatment period. CPAP adherence has often been assessed outside the context of adherence in other areas of medicine. In that context, CPAP adherence rates appear dismal.

However, in a prospective study of severe OSA patients investigating whether adherence or nonadherence to CPAP treatment predicted adherence to 3 well-known protective cardiovascular medications, CPAP adherence did not predict adherence with these medications. The adherence with the medications was not surprisingly low, given what is known about adherence (81-95% adherence to the medication). Again, with
severe OSA (AHI > 30) and comorbid heart disease, medication adherence was low, despite CPAP adherence.

In another study, patients who consistently refilled lipid-lowering medications were more adherent to CPAP. However, being married was the most powerful predictor of adherence. Once marital status entered the regression model, CPAP adherence and medication adherence were not significant predictors of adherence. This study demonstrates the complexity of the assessment of adherence.

A systemic review and meta-analysis by Bakker and Marshall examined the use of flexible pressure delivery of PAP. Although flexible pressure delivery intends to improve comfort and compliance through reduction of pressure during early exhalation, the study found that this flexible pressure modification does not significantly improve compliance with CPAP in patients with OSA.

Split-night PSG does not adversely affect short-term CPAP adherence in patients with OSA. Additionally, full-night PSG performed so patients can have a full night in the sleep disorders center to adapt to CPAP has not been shown to improve adherence. An individualized approach in which reasons for poor compliance are systematically investigated is essential to improving compliance. Poorly adherent patients should be asked about mask fit, mask leak, sinus/nasal congestion, mouth breathing, and general sleep habits to determine reasons for nonadherence.

Interventions to improve compliance include (1) attendance in a group clinic with education provided, (2) group cognitive behavioral therapy provided as two 1-hour sessions that include an educational talk and video of real CPAP users, (3) written literature and weekly phone calls during the first month of use, (4) use of nasal humidification, (5) alternative mask interfaces, and (6) prompt attention to adverse effects and nasal/sinus congestion. Patient education with sleep specialists has been shown to improve adherence. Patients who attended the authors’ short information
program showed higher daily usage and lower subjective daytime sleepiness. These results suggest that patients on CPAP therapy may benefit from education, even after a longer treatment period. Pressure-relief CPAP, a system that lowers the pressure at the onset of expiration, is hypothesized to improve adherence by reducing the uncomfortable sensation of breathing against high pressure while maintaining a patent upper airway. However, a review of the literature has not found that adherence to therapy is greater in patients using pressure-relief CPAP. Despite this, the author’s center frequently prescribes pressure-relief CPAP for all patients who require a setting of greater than 10 cm water.

Although an average of 20-40% of patients do not use the prescribed therapy, some sleep disorder centers have achieved greater than 90-95% adherence rates with CPAP therapy. In the authors’ experience, regular, close, and personalized follow-up greatly enhances adherence.

Complications and adverse effects

Pressure- and airflow-related complications include a sensation of suffocation or claustrophobia, difficulty exhaling, inability to sleep, musculoskeletal chest discomfort, aerophagia, and sinus discomfort. Pneumothorax and/or pneumomediastinum (extremely rare), pneumoencephalos (isolated case report), and tympanic membrane rupture (rare) also can occur.

Patients with claustrophobia may try using nasal pillows or behavioral management. If patients feel a sensation of increased resistance to expiration, use of a CPAP unit with a ramp feature is indicated. This unit permits the patient to fall asleep with little or no pressure applied, and the pressure gradually increases to the set optimal level over a predetermined interval (usually 15-30 min). BiPAP may be used as an alternative.

Mask-related problems include skin abrasions, rash, and conjunctivitis (due to air leaks). If excessive air leaks through the mouth, patients should use a chin strap to keep their mouths closed or they should try an oronasal mask. Consider consultation
with an otolaryngologist to rule out sinus dysfunction. If a poorly fitting mask causes skin breakdown and/or air leaks, patients should try masks of different sizes and/or models; a variety of interfaces are now available.

Nasal problems can include rhinorrhea, nasal congestion, epistaxis, and nasal and/or oral dryness. Nasal congestion can be treated with antihistamines and/or topical corticosteroids. Nasal dryness can be treated with topical saline sprays or humidification. If the air generated by the unit is too cold, the patient should use a heated humidifier.

**Medicare and Medicaid coverage**

For Medicare and Medicaid patients, regulations state that the coverage of CPAP is initially limited to a 12-week period for beneficiaries diagnosed with OSA as determined Centers for Medicare and Medicaid Services (CMS) criteria. CPAP is subsequently covered for those beneficiaries diagnosed with OSA whose OSA improved as a result of CPAP treatment during this 12-week period.
Airway Humidification

HUMIDITY AND HUMIDIFICATION

The prevention of cellular dehydration is a primary human homeostatic requirement. Complex and reliable mechanisms exist to maintain overall fluid balance.

Skin and other integuments are relatively impermeable to moisture, reducing evaporative water loss and consequent cooling. Special problems occur with specialised tissues (i.e., cornea, airways, lungs), and under abnormal conditions (e.g., burns, surgical procedures, some illnesses).

Anaesthetists need to maintain both global fluid balance and local tissue needs during anesthesia.

The purpose of this talk is to generally review evaporative water loss and consequent heat loss during anaesthesia, with particular emphasis on how this can be influenced by humidification of breathing circuit gases.

DEFINITIONS & PHYSICS

Vapour

Gas phase of a substance which is normally a liquid at ambient temperature and pressure.
Dalton’s Law

The pressure exerted by a mixture of gases or vapours enclosed in a given space equals the sum of the partial pressures that each gas or vapour would exert if it alone occupied the same space.

Saturated Vapour Pressure (SVP)

The saturated vapour pressure of a liquid is the partial pressure of the vapour above its liquid state at equilibrium, and is very dependent on the type of liquid and its temperature.

If a volatile liquid is introduced into a closed container, the pressure in the container will increase in proportion to the partial pressure of the vapour. In an expansile system the volume of gas increases (if the temperature is unchanged) because of the addition of the vapour and all constituents are proportionally diluted.

The SVP of water at 37°C is 47mmHg and contains 44mg/l of water whereas at room temperature (20°C) it is 20mmHg and contains only 18 mg/l).

**Table : Water Vapour, temperature, and SVP at 0, 20, and 37°C.**

<table>
<thead>
<tr>
<th>SVP at</th>
<th>0°C</th>
<th>20°C</th>
<th>37°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature (°C)</td>
<td>0</td>
<td>20</td>
<td>37</td>
</tr>
<tr>
<td>SVP (mmHg)</td>
<td>6</td>
<td>20</td>
<td>47</td>
</tr>
<tr>
<td>Content (mg/l)</td>
<td>5</td>
<td>18</td>
<td>44</td>
</tr>
</tbody>
</table>

Absolute Humidity

The absolute amount of water vapour in a gas expressed in either mg/l of gas mixture or mmHg (partial pressure).

Relative Humidity

Amount of water vapour in a gas expressed as a percentage of that which could be held by the gas if it were fully saturated at the same temperature, ie:

Relative Humidity = Actual Water Content / Water Content Fully Saturated %, or
Absolute Humidity = Actual Vapour Pressure / Saturated Vapour Pressure %

Relative Humidity is the common description of humidity used in weather reports as it correlates best with our perception of dryness or moistness of the air.

**Heat**

Heat is a form of energy that can be transferred from a warmer object to a cooler one and is related to the kinetic energy of vibration of molecules. Its units are Joules. 4.18 Joules equal one calorie and will raise one gram of water one degree centigrade. Total body heat production is about 80 Watts (ie Joules per second) for the average person (or 288 kJ/hr, 7,000 kJ/day, or about 1,700 kcal/day). Shivering can increase heat production up to four-fold, and exercise even more.

**Specific Heat**

Specific heat is the amount of heat required to raise the temperature of 1 kg of a substance by one degree Kelvin (the same as one degree centigrade); the units are Joules Kg\(^{-1}\) degK\(^{-1}\). The specific heat of water is 4.18 kJ per kg per °C, but it is often written as 1 kcal or 1 Cal kg\(^{-1}\) °C\(^{-1}\). Calories and calories should no longer be used. The specific heat of air is only 1.2 J litre\(^{-1}\) °C\(^{-1}\) ie 1/500th that of water.

**Heat Capacity**

This refers to the amount of heat required to raise the temperature of an object by one degree Kelvin. For a 70 kg patient this is about 245kJ per °C. As basal heat production is about 280kJ/hr it takes a little less than 1 hour to passively raise core temperature of a patient 1°C even if all losses are prevented.

**Specific Latent Heat of Evaporation**

The heat required to convert 1 kg of a liquid to its vapour at a given temperature. For water this is about 2.4 MJoules per kg at body temperature and only slightly greater at room temperature.
Measurement Of Humidity

Generally speaking this is very difficult.

Psychrometer

A system using two thermometers, one with a wet and the other a dry bulb. Air movement over the wet bulb causes evaporative cooling generating a difference in temperature readings.

This difference relates to the rate of airflow over the wet bulb and the relative humidity. Tables are used to look up the relative humidity from the two temperatures, however there is a high degree of inaccuracy. When the relative humidity is 100% there is no temperature difference.

Dewpoint Hygrometer

Using a precisely cooled shiny plate the user observes the temperature at which condensation first occurs. At this temperature the gas is fully saturated with water hence both the water content and the relative humidity at any other temperature can be ascertained from a vapour pressure table.

Weighing Water

By weighing anhydrous silica before and after exposure to a known volume of sample gas the water content of the sample can be determined. The silica must be kept away from other sources of moisture during weighing, and in practice this is a cumbersome and tedious technique.

The performance of active humidifiers is most simply tested by measuring the outlet temperature, the amount of water consumed per unit time, and the gas flow.

The relative humidity at the outlet of the humidifier under test (at this temperature and gas flow) can be established from the number of milligrams of water taken up per litre of gas. For example, 10 l/min at 37°C results in 600 litres of gas flow over one hour, and if each takes up 44 mg/l (to be fully saturated at
this temperature), 26.4g of water should have been used over the hour. If only 20mg was taken up, the relative humidity was 20/26.4 or 75.8%.

**Mass Spectroscopy**

Mass Spectroscopy can be very accurate but only if condensation (rain-out) does not occur in the sample line. This is the best technique for assessing “in-circuit” humidity as it can assess breath by breath changes.

**Humidity Transducers**

Special transducers are available in which the electrical conductivity of a membrane changes with water vapour pressure are available.

**Physiology Of Airway Humidification**

**Normal humidity in the airways**

While nose breathing at rest, inspired gases become heated to 36°C and are about 80% to 90% saturated with water vapour by the time they reach the carina, largely due to heat transfer in the nose. Mouth breathing reduces this to 60% to 70% relative humidity. Heat and moisture content falls from carina to nares, so that the nose is typically at 30°C.

A countercurrent mechanism of heat and moisture exchange in the airways maximises efficiency, with nasal cooling on inspiration and warming on exhalation. On very cold days while exercising a dripping nose is evidence of this. Tracheal temperature and humidity fall with increased ventilation particularly when the inspired gases are cold and dry.

**Heat and Water Loss**

If totally dry gases were inspired and fully saturated gases exhaled the total water loss from ventilation at rest would be about 300 ml/day in the average adult. Normally about half is retained thanks to the efficiency of the nose (30% saving) and the
humidity of inspired room air (25% saving). Bypassing the nose with an ETT and not humidifying gases cases maximal losses.

Non-respiratory water losses are typically 300 to 600 ml/day but are increased if warm moist surafces are exposed (ie burns, open abdomen) particularly if the operating theatre is cold and has high flow airconditioning.

Heat losses are the result of four primary processes:
- Radiation 40% (depends on clothing; 4th power of absolute temp diff 10°C = 18%)
- Convection 30% (increased in windy environments)
- Evaporation 20% (ie, from skin)
- Respiration 10% NB: 8% water evaporation, 2% heating Air

Respiratory losses of both heat and water increase with increased ventilation, hyperthermia, and dry inspired gases.

Advantages Of Humidification

Reduced heat loss

Heat loss from warming inspired air from 20 deg.C to 37 °C:
= Ventilation x Specific Heat Air x Temp rise
= 7 litre min-1 x 1.2 Joule litre-1 deg.C x 17 °C
= 142.8 Joule min-1 (or 8.6 kJoule per hour or 2.38 watts)

Thus warming the inspired air from 20 °C requires only about 3% of the body’s normal heat production and at maximum could only cool a non-heat producing body mass by 0.035 °C per hour.

Heat loss from humidifying exhaled air fully saturated at 37°C:
= Ventilation x Water required x Specific latent heat of vapourisation
= 5 litre min-1 x 44 mg litre-1 x 2.4 MJoule kg-1
= 528 Joule min-1 (or 31.7 kJoule per hour or 8.8 watts)
Hence in the worst case (completely dry inspired gases and, no countercurrent benefits), humidification about 11.3% of the body’s heat production.

Thus fully humidifying completely dry warm air requires four times as much heat as warming it alone. Even so, in the worst case at rest, the total rate of body cooling would be only 0.16 °C per hour from ventilation.

If a 70% efficient HME was used the total heat loss would only be 0.05 °C per hour and the total heat loss from ventilation over a 10 hour period would be only half a degree. In contrast, rapidly infusing one litre of water at 20 °C would cool the patient by 0.3 °C almost immediately.

Note that respiratory heat loss increases if the inspired air is very cold or ventilation is increased considerably, for example exercise at high altitudes.

Very importantly neonates and infants have metabolic rates (and hence ventilatory requirements) approximately 2 to 3 times that of adults on a weight basis. They stand to lose a lot more heat relative to their heat capacity (body mass) and hence will cool down 2 to 3 times quicker from ventilation. Neonates stand to lose 0.3 to 0.5 °C per hour from respiratory heat loss (more if hyperventilated) unless gases are humidified.

Consequently in adults either 70% humidification of inspired gases for 10 hours or no humidification for 3 hours result in possible total temperature falls of only 0.5 °C. Radiant heat loss and heat loss from room temperature fluid infusions far exceeds this is clinical practice. Unless there are other potential or actual problems with hypothermia, or to avoid excessive drying of secretions, using any form of humidification in adults for procedures of 2 to 3 hours duration is unjustified, in my opinion.

In neonates, however, respiratory heat loss may be significant even during short periods of ventilation.

A small but important practical point is that body temperature should be measures from a wedged nasal rather than oesophageal
temperature probe, as oesophageal probes tend to measure endotracheal tube rather than patient temperature.

**Reduced water loss**

During anaesthesia it is easy to replace the small respiratory water loss with iv fluids. Prolonged extreme exertion as in fun runs and mountaineering may cause significant dehydration from respiration and adequate fluid intake is essential.

**Prevention of cilial damage and reduced drying of secretions**

Cilial paralysis and reduced rates of mucus flow occur below 50% relative humidity at 37 °C, but how long it takes for irreversible and/or significant changes is not known. During brief general anaesthetics this is not a problem. Prolonged severe dehydration of the bronchial tree leads to encrustation of mucus and bronchial or endotracheal obstruction, particularly in neonates and patients with respiratory infection.

Recommendations for humidification of inspired gases on this basis are generally anecdotal.

**Microbial Filtration**

Some HME’s incorporate viral/bacterial filters.

**Disconnection**

All humidifiers increase the component count in the breathing circuit and increase the risk of disconnection. Heated humidifiers commonly require actively heated delivery tubes and these may be heavy and bulky or use non-standard connectors. Much less of a problem with HME’s although some have non-standard connectors or are quite bulky.

**Overheating**

An uncommon event with modern servo controlled active humidifiers, although burns from the delivery hose have been recently reported. Impossible with HME’s.
Overhydration

Usually only a problem with nebuliser type devices. Impossible with HME’s.

Circuit resistance, deadspace, and circuit compliance changes

Most modern HME’s cause a small increase in resistance to gas flow, typically 2 cm H20 at 40 l/min (a typical inspiratory flow rate during anaesthesia). Obstruction of HME’s with mucus or as a result of expansion of saturated heat exchanging material may occur and can result in dangerous increases in resistance. Heater humidifiers also increase circuit resistance but usually to a lesser extent (provided that tubing of adequate diameter is used). Bubble-through humidifiers cause obvious increases in resistance. Rainout may cause obstruction of breathing tubes.

Deadspace considerations in HME’s limit their performance but not their clinical utility. Greater mass of heat exchanging material improves performance (especially with larger tidal volumes) but the deadspace increases as well, so usually it is necessary to choose the right size HME to suit the patient.

Increased circuit compliance is important to consider when ventilating neonates.

Infection

Not a problem with disposable HME’s, but can occur in ICU with the water bath of heated humidifiers.

Drowning

Possible on tilting the water bath of some heater humidifiers, particularly for neonates on continuous flow circuits. Can’t occur with HME’s.

Interference with other devices

Excessive humidity in the proximal breathing circuit from heated humidifiers may interfere with sampling (side-stream) type CO2 analysers and condensation may affect the reading on some
Airway Humidification

tidal volume meters. Rain-out from active humidifiers may be a considerable problem, particularly in ICU’s.

Inadequate humidification

HME’s are probably inadequate for:
- Prolonged ICU use, ie more than 2 to 3 days
- More than 6 hours or so where respiratory secretions are a problem
- Warming cold patients
- Hyperventilation.

Active heater humidifiers can provide 100% relative humidity at 37 °C or more for prologed periods and are preferable in the above situations.

Cost

Disposable HME’s cost $2.00 to $7.00 per patient. A F&P type dome costs $25.00, and as well as the capital cost of the base, the delivery tube will have to be sterilised at the end of the case.

METHODS OF HUMIDIFYING INSPIRED GASES

Anaesthetic circuits

Water’s to and fro type systems generate warm moist gases but are little used these days. Bain type circuits result in both countercurrent heating of the inspired gases and rebreathing of exhaled gas for some humidification, but they probably only are about 10% to 20% efficient on IPPV and even less when used for spontaneous breathing (because of the high fresh gas flows required). Circle circuits warm up after a period of time and do generate water but again are relatively little help.

Nebulisers

Rarely used these days as they nebulisation process results in an inhaled aerosol of 100% relative humidity at lower than room temperature, which increases heatloss rather than reducing it.
Water uptake may be excessive and there is a real potential for infection from the water bath. Used only to liquefy secretions, but these days active humidification is far preferable.

**Heat and Moisture Exchangers (HME’s)**

Initially made for tracheostomied patients from copper mesh ("Swedish nose"). Now most are cheap and disposable and made from modified hygroscopic paper filters encased in a plastic case.

HME’s are usually 50% to 80% efficient at best (depending on inspired humidity), consequently heat and water loss and dehydration of respiratory secretions still occur, particularly if the inspired gases are completely dry. Efficiency is reduced further by large tidal volumes or by failure to place the HME right on the endotracheal tube, permitting rain-out. Full function is not immediate, typically taking 5 to 20 minutes to achieve steady state.

None the less they are almost as effective as the human nose and provide enough humidification to maintain ciliary action and mucus flow and to reduce heat and moisture losses during anaesthesia to insignificant levels. The Pall filter is also one of the best bacterial filters on the market. They are simple to use, cheap, act as a macroscopic particle trap and avoid many of the problems associated with active humidifiers.

**Active Heated Humidifiers**

These electrically powered heated water bath devices are capable of fully saturating and heating inspired gases to 37 °C at high flow rates (ie to 60 l/min) and in this regard are far superior to HME’s. A heated delivery hose is required to prevent cooling and loss of humidity in the inspiratory limb of the circuit. Sterile single use water chambers with wicks are common, and some are automatically filled from a water reservoir.

They have many disadvantages, including cost, storage requirements, servicing, circuit complexity, water rain-out leading to monitor malfunction or tubing occlusion, extra risk of
Airway Humidification

disconnection, infection hazard, potential for burns and drowning, and altered circuit compliance.

RESPIRATORY GAS HUMIDIFICATION

Basics

Respiratory gas humidification is a method of artificially conditioning respiratory gas for the patient during therapy, and involves humidification, warming, and occasionally filtration of the gas being delivered.

If these three measures are not performed to compensate for the natural conditioning of air by the respiratory system, pulmonary infections and lung tissue damage may occur. This is particularly problematic in high gas-flow therapies such as mechanical ventilation, in patient populations with highly sensitive respiratory tracts (i.e. asthmatics), or among those requiring ventilation for longer periods of time.

The two methods currently available for this purpose are active or passive respiratory gas humidification.

Active respiratory gas humidifiers

An active respiratory gas humidifier ensures that patients on mechanical ventilation are supplied with optimally conditioned respiratory gas. In active humidifying processes, moisture and heat is input to respiratory gas by an electrically powered humidifier. Performance data and safety-related requirements for active respiratory gas humidifiers are specified by the standard ISO 8185. According to that standard, the minimum water content of inspired respiratory gas is ca. 33 mg/dm³ and the maximum respiratory gas temperature is ca. 42 °C.

The aggregation of water in the gas produced by an active respiratory gas humidifier may be a suspension, or aerosol, which is produced by a nebulizer; or particulate water, output from an evaporator or bubble humidifier.
Nebulizers

Nebulizers generate aerosols consisting of droplets of various sizes that are admixed to the inspired respiratory gas. Types of nebulizers currently on the market include

1. Small Volume Nebulizers, which are used to administer medications such as salbuterol or albuterol.
2. Large Volume Nebulizers, which are similar to bubble humidifiers except for the addition of an air entrainment port, and
3. Ultrasonic Nebulizers, which may carry a risk of overwatering the patient.

The high density mist produced by nebulizers is useful in decreasing the viscosity of respiratory secretions in those suffering from conditions such as cystic fibrosis, croup, epiglottitis, and bronchiectasis.

Evaporators

Evaporators enrich the inspired respiratory gas with water vapor. In a throughflow evaporator, the inspiration flow is led through a warmed up water bath, in case of a surface evaporator however the inspiration flow is guided along the surface of the water level. Consequently, a surface evaporator transports only water vapor and no water droplets into the patient. The advantage of it is, water vapor doesn’t carry any germs. Therefore, the risk of passing on germs by surface evaporators is a minimum.

Bubble Humidifiers

In a bubble humidifier, or bubble bottle as they are affectionately known by respiratory therapists, the inspiration flow is guided through a capillary system. In this capillary system warmed up water is circulating. Although the humidifying capacity of a bubble respiratory gas humidifier is rather low, it may be improved by increasing the water temperature. A bubble bottle is mostly used in oxygen therapy with high flow rates via a mask.
or nasal cannula in order to prevent drying of the mucous membranes in the nose and mouth.

**Passive Respiratory Gas Humidifiers**

Passive respiratory gas humidifiers are independent from any external energy source or external water supply. They function as heat and moisture Exchangers (HME) and are placed like an artificial nose between a tube and Y piece. Here they withdraw heat and moisture from expirations, which they resupply to the inspired gas during the following inspiration. As there are significant functional differences among the various HMES on the market, respiratory therapists should test the efficacy of each individual model. The ideal HME has high reversible water retention capacity, small internal volume, and low flow resistance.

To enable the absorption of sufficient amounts of water and heat, the expiratory stream of respiratory gas must be fully filtered through the HME. Leakages in the system, such as may be caused by bronchial fistulae, will render this system less effective. Other negative effects of this technology include increased secretions (i.e. mucus) and nosebleeds, either or which may clog an HME. In such cases, the application of active respiratory gas humidifiers is recommended.

**TYPES OF HUMIDIFIERS**

Humidifiers are devices that add molecules of water to gas. They are classified as active or passive based on the presence of external sources of heat and water (active humidifiers), or the utilization of patients’ own temperature and hydration to achieve humidification in successive breaths (passive humidifiers).

**Active Humidifiers**

Active humidifiers act by allowing air passage inside a heated water reservoir. These devices are placed in the inspiratory limb of the ventilator circuit, proximal to the ventilator. After the air is loaded with water vapor in the reservoir, it travels along the
inspiratory limb to the patient’s airway. As condensation of water vapor may accumulate as the surrounding temperature of the inspiratory limb decreases, these systems are used with the addition of water traps, which require frequent evacuation to avoid risk of contamination of the circuit.

A diagram of a heated humidifier that operates at 50°C to achieve an AH of 84 mg/L at the side of the humidifier but achieves only an AH of 44 mg/L due to significant condensate in the tubing. Due to the aforementioned shortcoming, heated humidifiers are usually supplied with heated wires (HWH) along the inspiratory limb to minimize this problem.

These humidifiers have sensors at the outlet of the humidifier and at the Y-piece, near the patient. These sensors work in a closed-loop fashion, providing continuous feedback to a central regulator to maintain the desired temperature at the distal level (Y-piece). When the actual temperature exceeds or decreases beyond certain extreme level, the alarm system is triggered.

Even though the ideal system should permit autocorrections based on humidity levels, commercially available sensors provide feedback based on changes in temperature. An active humidifier with a heated wire in the inspiratory limb; both temperature sensors, one at the side of the patient and the other at the outlet of the heated reservoir, are shown. Usual temperature setting for the current heated humidifiers is 37°C.

The performance of humidifiers may be affected by room temperature, as well as patient minute ventilation. In the last situation, an increase in minute ventilation preserving the same temperature of the heated reservoir may not be adequate to deliver appropriate AH to the patient. Therefore, some humidifiers are supplemented with automatic compensation systems, which compute the amount of thermal energy needed to humidify certain volume of gas and change the temperature of the water reservoir accordingly. Lellouche et al. studied the performance of two HWHs and HH devoid of heated wires under different room temperatures (high, 28–30°C; normal, 22–24°C). The authors also investigated
device performance by changing the temperature of gas within the ventilators and under two different minute ventilation levels (Ve) (low of 10 L/min and high of 21 L/min). The presence of high minute ventilation and room temperature resulted in a reduction of humidification performance, with absolute humidity of less than 20 mg H₂O/L. One of the tested humidifiers had an automatic compensation system for changes in minute ventilation. This model achieved higher AH levels than those that relied only on temperature sensors. Furthermore, other studies have also reinforced the effect of room temperature, variance in minute ventilation, and ventilator gas temperature on levels of absolute humidity delivered to patients. Notably, some studies indicate that heated humidifiers without heated wires achieve higher levels of humidification than HWHs. Nevertheless, it is clear that they are associated with more condensation and respiratory secretions. Hence, these types of humidifiers are becoming increasingly unpopular among respiratory care providers. As previously mentioned, inspiratory heated wires can minimize condensation. However, exhaled air can form rainout in the expiratory limb. This has led to the utilization of double heated wire (DHW) circuits. This practice has replaced the use of single heated wires (SHW) circuits in some countries. Another described technique to limit condensate in the expiratory limb is to use porous expiratory circuits.

Heated humidifiers have different designs and different techniques for humidification. Accordingly, these devices are classified as (1) bubble; (2) passover; (3) counter-flow; and (4) inline vaporizer.

(1) Bubble. In bubble humidifiers, gas is forced down a tube into the bottom of a water container. The gas escapes from the distal end of the tube under water surface forming bubbles, which gain humidity as they rise to the water surface. Some of these humidifiers have a diffuser at the distal end of the tube that breaks gas into smaller bubbles. The smaller the bubbles, the larger the gas-water interface
allowing for higher water vapor content. Other factors that influence water vapor content of the produced gas are the amount of water in the container and the flow rate. Simply, the higher the water column in the container, the more gas-water interface will ensue, so water levels should be checked on a frequent basis. In terms of flow rate, when slow flows are delivered, there is more time for gas humidification. Bubble humidifiers may be unheated or heated. Typically, unheated bubble humidifiers are used with low-flow oral-nasal oxygen delivery systems. Heated bubble humidifiers provide higher absolute humidity. They are designed to work with flow rates as high as 100 L/min. These humidifiers usually use diffusers to increase the liquid-air interface. A problem with heated bubble humidifiers is that they exhibit high resistance to airflow imposing higher work of breathing than passover ones. Furthermore, they may generate microaerosol. Nevertheless, the CDC guidelines for prevention of health care associated pneumonia reported that the amount of aerosol produced by these types of humidifiers may not be clinically significant. Despite this statement, the use of bubble humidifiers during mechanical ventilation has fallen in favor of passover ones.

(2) Passover. In passover humidifiers, gas passes over a heated water reservoir carrying water vapor to the patient. These are typically used for the purpose of invasive and noninvasive mechanical ventilation. Another variant of passover humidifiers is the wick one. In this type of device, the gas enters a reservoir and passes over a wick that acts as a sponge that has its distal end immersed in water. The wick pores provide more gas-water interface allowing for more humidification compared to simple passover humidifiers. The water reservoir is fed through a closed system. This system can be supplied with water either manually through a port or float feed system that ensures
the water level remains constant all the time. As dry gas enters the chamber and travels through the wick, heat and moisture increase. Due to the fact that gas does not emerge underneath the water surface, no bubbles are generated. A third type of passover humidifier involves a hydrophobic membrane. As with the wick device, dry gas passes through a membrane. Nevertheless, its hydrophobic characteristic only allows passage of water vapor, precluding liquid water to travel through it. Similarly to the wick humidifier, bubbles and aerosols are not generated. As mentioned previously, these humidifiers are more commonly used during mechanical ventilation than bubble ones due to their lower flow resistance and absence of microaerosols. In all cases, a temperature probe is placed near the Y piece of the ventilator circuit to ensure delivery of gas with optimal temperature. As it was stated above, the presence of condensate in the tubing may increase resistance, which can decrease volume delivered in pressure controlled, or increase peak pressure in volume controlled modes. Despite the need of the aforementioned heated wires to avoid undesirable condensation, it is also worth mentioning that use of these wires does not come without thermal risks. Consequently, the American Association of Respiratory Care (AARC) clinical practice guidelines recommend gas delivery with a maximum temperature of 37°C and 100% RH (44 mg H₂O/L).

In terms of humidifier heating systems, currently there are 6 types of devices. The hot plate element, which sits at the bottom of the humidifier, is one of the most commonly used. Other devices include the wraparound element, which surrounds the humidifier chamber; a collar element, which sits between the reservoir and the outlet; the immersion heater, which is placed directly inside the water reservoir; and the heated wire, which is placed in the inspiratory limb of the ventilator.
(3) Counter Flow. In the recently described counter-flow humidifier, water is heated outside the vaporizer. After being heated, water is pumped to the top of the humidifier, enters the inside of the humidifier through small diameter pores, and then runs down a large surface area. Gas flows in counter direction. During its passage through the chamber of the humidifier, the air is moisturized and warmed to body temperature. Schumann et al. compared the counter-flow humidifier, a heated passover, and a heat and moisture exchanger (HME) in an artificial lung model. The authors demonstrated that the counter-flow device imposed less work of breathing compared with the other ones. In addition, the humidification performance of the counter-flow model was independent of flow and respiratory rate, in contrast to the heated passover humidifier in which humidification performance decreased with increasing ventilator rates. This technology is promising but more studies are needed before it becomes widely adapted.

(4) Inline Vaporizer. The novel inline vaporizer uses a small plastic capsule where water vapor is injected into the gas in the inspiratory limb of the ventilator circuit immediately proximal to the patient wye. In addition to the water vapor, gas heating is supplemented by a small disk heater in the capsule. Water is delivered to the capsule by a peristaltic pump housed in a controller. The amount of water sent to the capsule is set by the clinician based on minute volume through the circuit. Both temperature and humidity are adjustable and displayed constantly. The proximity to the wye connection obviates the requirement for heated wires and external temperature probes. The manufacturer reports very high AH production with this system. However, this system was only studied during high frequency percussive ventilation.
Passive Humidifiers

Heat and Moisture Exchangers HMEs

Heat and moisture exchangers are also called artificial noses because they mimic the action of nasal cavity in gas humidification. They operate on the same physical principle, as they contain a condenser element, which retains moisture from every exhaled breath and returns it back to the next inspired breath. Unlike heat humidifiers, which are placed in the inspiratory limb of the circuit, these devices are placed between the Y piece and the patient. This may increase resistance to airflow not only during inspiration, but also during the expiratory phase.

In situations in which administration of aerosolized medications is needed, HMEs need to be removed from the circuit to avoid aerosol deposition in HME filters. Otherwise, HMEs with capability to change from “HME function” to “aerosol function” should be used. Initial designs of HMEs used condensers made of metallic elements that had high thermal conductivity. Thus, they were able to recapture only 50% of the patient’s exhaled moisture. Hence, they provided humidification of 10–14 mg H₂O/L, at tidal volumes (VT) ranging between 500 mL and 1000 mL. These devices were known as simple HMEs. They were not disposal and created a significant resistance during mechanical ventilation.

Newer designs of HMEs include hydrophobic, combined hydrophobic hygroscopic, and pure hygroscopic HMEs. In hydrophobic HMEs, the condenser is made of a water repelling element with low thermal conductivity that maintains higher temperature gradients than in the case of simple HMEs. In combined hydrophobic hygroscopic HMEs, a hygroscopic salt (calcium or lithium chloride) is added inside the hydrophobic HME. These salts have a chemical affinity to attract water particles and thus increase the humidification capacity of the HME. Pure hygroscopic HMEs have only the hygroscopic compartment. During exhalation, vapor condenses in the element as well as in
the hygroscopic salts. During inspiration, water vapor is obtained from the salts, obtaining an absolute humidity ranging between 22 and 34 mg H₂O/L. The basic structure and work principle of HMEs.

Hydrophobic HMEs were found to cause more narrowing in ETT diameter compared to hygroscopic ones. Therefore, the aforementioned HMEs are not frequently used. Filters can be added to either hydrophobic or hygroscopic HMEs resulting in a heat and moisture exchanging filter (HMEF). These filters operate based on electrostatic or mechanical filtration. Specifically, based on the predominant mechanism applied, these filters may be classified into pleated or electrostatic filters.

The pleated filters have more dense fibers and less electrostatic charges, whereas the electrostatic filters have more electrostatic charges and less dense fibers. Pleated filters function better as barriers to bacterial and viral pathogens than electrostatic filters. However, they confer higher airflow resistance.

The pleated nature of the membrane causes a turbulent airflow, which increases the pathogen’s deposition onto the inside of the filter. The electrostatic filters are subjected to an electric field. Since bacteria and viruses carry electric charges, they get trapped within the electric field of these filters. These filters usually have larger pores than the pleated membranes, and they rely mainly on the electrostatic mechanism. The previously described filter confers little to the humidification process and increases resistance. Therefore, they are mainly used as barriers to pathogens. HMEs design and performance standards are defined by the International Organization for Standardization (ISO). According to these standards, the appropriate HME should have at least 70% efficiency, providing at least 30 mg/L of water vapor. In a recent study, Lellouche and colleagues independently assessed the humidification capacity of 32 HMEs. Strikingly, 36% of tested HMEs had an AH of 4 mg H₂O/L lower than what was listed by the manufacturer. In fact, in some of them the difference was higher than 8 mg H₂O/L.
Airway Humidification

Intuitively, as HMEs eliminate the problem of tubing condensation, it may be considered as “elements of choice” to prevent ventilator-associated pneumonia (VAP). Nevertheless, whether the presence of tubing condensate represents an important factor for the development of VAP in well-maintained circuits remains controversial. Furthermore, HMEs also present some shortcomings. Specifically, impaction of secretions or blood within the device may increase airway resistance and work of breathing. In extreme circumstances, complete airway obstruction has been reported. Therefore, patient selection becomes an essential component in the use of HMEs.

In certain devices, an active heated water source can be added to HMEs converting them from passive to active, increasing their humidification capacity. If the external source of water runs out, these devices will still work as passive HMEs. Several models exist, including the Booster, the Performer, the Humid Heat, and the Hygrovent Gold.

In the Booster model, the heating unit is incorporated between the HME and the patient. During inspiration the gas passes through the HME carrying water vapor based on the passive operation of the HME and then the heating unit adds to the humidity content of the gas before it reaches the patient. As water enters the HME-Booster, it saturates the hydrophobic membrane contained in it. The moisture in the saturated membrane is then heated by the positive temperature control element connected to it. It is thought that the utilization of this device may increase AH by 2-3 mg/L of H2O more than passive HMEs.

The Performer device is characterized by a metal plate in the middle of the HME, in between two hydrophobic and hygroscopic membranes. This metal plate is heated by an external source that has three sets of temperature to deliver 40°C, 50°C, and 60°C. A water source provides it to one end of the humidifier. The water reaches the two membranes and the metal plate heats it. Then, the water evaporates augmenting vapor content in the inspired gas. The performer is able to deliver AH of 31.9 to 34.3 under
normothermic conditions. The Humid Heat is a hygroscopic HME that has an external heating source with the water being added at the patient side. In one bench study, it was found to provide an absolute humidity of 34.5 mg H2O/L. Humid Heat has preset values for temperature and humidity. The only parameter that needs to be set is the value of minute volume of the ventilator, making its use very simple.

The Hygrovent Gold is an active hydrophobic HME that has an adapter to which a heating element can be inserted and a water line to supply water inside the HME. There is a thermal sensor to avoid overhumidification. Under normothermic conditions, it was reported to provide an AH of 36.3 mg H2O/L. Increased flow resistance can be found with these active humidifiers, which is likely related to accumulation of water condensate in the passive component.

Last, another active HME model is based on chemical reactions. In these HMEs, the carbon dioxide in the exhaled breath is exploited to generate heat through a chemical reaction when it passes through the humidifier. Broach and Durbin Jr. conducted a randomized controlled clinical trial on fifty patients undergoing coronary artery bypass grafting and compared between chemically heated HME and the conventional passive ones. The chemically heated HME resulted in more rapid rewarming of mildly hypothermic patients, with no difference in clinical outcomes. Due to limited experience with this device, chemically active HMEs are not currently used in clinical practice.
Respiratory mechanics refers to the expression of lung function through measures of pressure and flow. From these measurements, a variety of derived indices can be determined, such as volume, compliance, resistance, and work of breathing (WOB). Waveforms are derived when one of the parameters of respiratory mechanics is plotted as a function of time or as a function of one of the other parameters. This produces scalar tracings of pressure-time, flow-time, and volume-time graphics, as well as flow-volume and pressure-volume (P-V) loops.

All current-generation positive-pressure ventilators provide some monitoring of pulmonary mechanics and graphics in real time at the bedside. When interpreting these measurements, it is important to remember that bedside monitoring of mechanics and graphics during positive-pressure ventilation portrays the lungs as a single compartment and assumes a linear response over the range of tidal volume ($V_T$).

Although this is a physiologic oversimplification, the information nonetheless is useful to evaluate lung function, assess response to therapy, and optimize mechanical ventilator support. An evaluation of respiratory mechanics allows the best available
evidence to be individualized to the patient. By necessity, any
discussion of respiratory mechanics involves mathematics.
Fortunately, much of the mathematics is basic algebra, and for the
most part, I will stick to that in this chapter.

PRESSURE

Airway Pressure

Airway pressure is measured universally during mechanical
ventilation. Pressure is measured ideally at the proximal airway,
but most ventilators do not because proximal airway pressure
monitoring exposes the sensor to secretions and carries other
technical issues. Alternatively, the ventilator can measure pressure
proximal to the expiratory valve during the inspiratory phase to
approximate inspiratory proximal airway pressure, and it can
measure pressure distal to the inspiratory valve during the
expiratory phase to approximate expiratory proximal airway
pressure. Because flow in the expiratory limb is zero during the
inspiratory phase and flow in the inspiratory limb is zero during
the expiratory phase, pressures measured in this manner should
approximate proximal airway pressure.

Airway pressure is typically displayed on the ventilator screen
as a function of time. The shape of the airway pressure waveform
is determined by flow and \( V_t \) from the ventilator, lung mechanics,
and any active breathing efforts of the patient.

Equation of Motion

Airway pressure is predicted mathematically by the equation
of motion: (1) where \( P_{\text{vent}} \) is the proximal airway pressure applied
by the ventilator, \( P_{\text{mus}} \) is the pressure generated by the patient’s
inspiratory muscles, \( V_t \) is tidal volume, \( C_{\text{rs}} \) is respiratory system
compliance, \( R_{\text{aw}} \) is airway resistance, \( V_t \) is inspiratory flow, PEEP
is the PEEP set on the ventilator, and PEEP\(_i\) is intrinsic PEEP (auto-
PEEP). The inerance variable, representing the effect of inertia,
is assumed to be low and thus disregarded.
R_{aw} and C_{RS} can be obtained by fitting the equation of motion to P, V, and \(\dot{V}\) with a multiple linear regression analysis, called linear least-squares fitting. This approach is incorporated into the software of some ventilators, allowing display of \(R_{aw}\), \(C_{RS}\), and auto-PEEP without the need for inspiratory and expiratory pause maneuvers. P, V, and \(\dot{V}\) are digitized at 100 Hz, allowing \(R_{aw}\) and \(C_{RS}\) be calculated from 100 or more equations per breath. This method can be applied during the whole breathing cycle or only in the inspiratory or expiratory phase, although restricting the analysis to the inspiratory phase may be more appropriate in patients with COPD who have flow limitation. The least-squares fitting method assumes that \(P_{mus}\) is zero and is thus less valid if the patient is actively breathing. An important methodological issue is that the least-squares fitting approach uses a single linear model that does not take into account changes of \(R_{aw}\) and \(C_{RS}\) with lung volume, and it also neglects flow turbulence and inertial forces.

### Alveolar Pressure

During volume control ventilation, alveolar pressure (\(P_{alv}\)) at any time during inspiration is determined by the volume delivered and \(C_{RS}\): \(P_{alv} = \frac{V}{C_{RS}} + PEEP\). For pressure control ventilation, \(P_{alv}\) at any time after the initiation of inspiration is: \(P_{alv} = \Delta P \times (1 - e^{-t/\tau}) + PEEP\), where \(\Delta P\) is the pressure applied to the airway above PEEP, e is the base of the natural logarithm, t is the elapsed time after initiation of the inspiratory phase, and \(\tau\) is the time constant.

### Plateau Pressure

Due to \(R_{aw}\), proximal airway pressure will always be greater than \(P_{alv}\) during inspiration if flow is present. \(P_{alv}\) is estimated with an end-inspiratory hold maneuver. Plateau pressure (\(P_{plat}\)) is measured during mechanical ventilation by applying an end-inspiratory breath-hold for 0.5–2 s, during which pressure equilibrates throughout the system, so the pressure measured at the proximal airway approximates the \(P_{alv}\).
Airway pressure and flow waveforms during constant flow volume control ventilation, illustrating the effect of an end-inspiratory breath-hold. With a period of no flow, the pressure equilibrates to the plateau pressure (P\text{plat}). P\text{plat} represents the peak alveolar pressure. The difference between P\text{z} and P\text{plat} is due to time constant inhomogeneity within the lungs. The difference between the peak inspiratory pressure (PIP) and P\text{plat} is determined by resistance and flow. The difference between P\text{plat} and PEEP is determined by tidal volume and respiratory system compliance. P\text{z} = pressure at zero flow.

With rapid airway occlusion at the end of inspiration, flow drops to zero, and the proximal airway pressure immediately decreases to a lower level (the pressure at zero flow). R\text{aw} and end-inspiratory flow determine the difference between peak inspiratory pressure (PIP) and P\text{z}. During airway occlusion, pressure further declines to reach a plateau (P\text{plat}). The difference between P\text{z} and P\text{plat} is determined by time constant heterogeneity within the lungs (ie, pendelluft) and the viscoelastic behavior of the stress relaxation of the pulmonary tissues. Measurement of P\text{plat} is valid only during passive inflation of the lungs, but not during active breathing. During pressure control ventilation, the flow might decrease to zero at the end of the inspiratory phase; if this occurs, PIP and P\text{plat} are equal.

P\text{plat} is determined by V\text{T} and C\text{RS} during full ventilatory support: P\text{plat} = V\text{T}/C\text{RS}. A high P\text{plat} indicates risk of alveolar over-distention. P\text{plat} should ideally be kept at $\approx 30$ cm H$_2$O, with some evidence suggesting that P\text{plat} should be targeted to $< 25$ cm H$_2$O in patients with ARDS. This assumes that chest-wall compliance (C\text{CW}) is normal. A high P\text{plat} may be safe (and necessary) if C\text{CW} is decreased.

A method has been described that uses the expiratory time constant ($\dot{\delta}_E$) to provide real-time determinations of P\text{plat} without the need for an end-inspiratory pause maneuver. Using this approach, $\dot{\delta}_E$ is estimated from the slope of the passive expiratory flow curve between 0.1 and 0.5 s. P\text{plat} is then calculated as: (2)
This approach has the advantage of being able to be used in spontaneous breathing modes such as pressure support, but has the disadvantage of requiring a computerized algorithm to make the necessary calculations.

**Auto-PEEP**

Incomplete emptying of the lungs occurs if the expiratory phase is terminated prematurely. The pressure produced by this trapped gas is called auto-PEEP, intrinsic PEEP, or occult PEEP. Auto-PEEP increases end-expiratory lung volume and thus causes dynamic hyperinflation.

Auto-PEEP is measured by applying an end-expiratory pause for 0.5–2 s. The pressure measured at the end of this maneuver in excess of the PEEP set on the ventilator is defined as auto-PEEP. For a valid measurement, the patient must be relaxed and breathing in synchrony with the ventilator, as active breathing invalidates the measurement. The end-expiratory pause method can underestimate auto-PEEP when some airways close during exhalation, as may occur during ventilation of the lungs of patients with severe asthma. In spontaneously breathing patients, measurement of esophageal pressure ($P_{es}$) can be used to determine auto-PEEP.

Auto-PEEP is a function of ventilator settings ($V_T$ and expiratory time) and lung function ($R_{aw}$ and lung compliance): auto-PEEP = $V_T / (C_{RS} \times (e^{kx \times T_E} - 1))$, where $Kx$ is the inverse of the $\delta_E (1/\delta)$. Note that auto-PEEP is increased with increased resistance and compliance, increased breathing frequency or increased inspiratory time ($T_i$; both decrease $T_E$), and increased $V_T$. Clinically, auto-PEEP can be decreased by decreasing minute ventilation (rate or $V_T$), increasing $T_E$ (decreasing rate or $T_i$), or decreasing $R_{aw}$ (eg, bronchodilator administration).

**Mean Airway Pressure**

Mean airway pressure ($P_{aw}$) is determined by PIP, the fraction of time devoted to the inspiratory phase ($T_i / T_{tot}$, where $T_{tot}$ is total...
respiratory cycle time), and PEEP. For constant flow-volume ventilation, in which the airway pressure waveform is triangular, \( P_{aw} \) can be calculated as: 
\[
P_{aw} = 0.5 \times (\text{PIP} - \text{PEEP}) \times \left( \frac{T_I}{T_{tot}} \right) + \text{PEEP}
\]
During pressure ventilation, in which the airway pressure waveform is rectangular, \( P_{aw} \) can be estimated as: 
\[
P_{aw} = (\text{PIP} - \text{PEEP}) \times \left( \frac{T_I}{T_{tot}} \right) + \text{PEEP}
\]
The mean \( P_{alv} \) may be different than \( P_{aw} \) if the inspiratory airway resistance (\( R_I \)) and expiratory airway resistance (\( R_E \)) are different, which is often the case in lung disease: 
\[
\text{mean } P_{alv} = P_{aw} + \left( \frac{V_E}{60} \right) \times (R_E - R_I)
\]
where \( V_E \) is expiratory flow.

**Esophageal Pressure**

Pleural pressure (\( P_{pl} \)) cannot be easily measured directly. The traditional approach to assess \( P_{pl} \) is the use of an esophageal balloon, which consists of a thin catheter with multiple small holes in the distal 5-7 cm of its length. A 10-cm-long balloon is placed over the distal end of the catheter to prevent the holes in the catheter from being occluded by esophageal tissue and secretions, and the balloon is inflated with a small amount of air (0.5 mL). The proximal end of the catheter is attached to a pressure transducer.

The catheter is inserted orally or nasally to <“35-40 cm from the airway opening. Correct positioning of the esophageal balloon is necessary to ensure accurate \( P_{es} \) measurements. After the balloon is inflated and the pressure is measured, the \( P_{es} \) waveform should be compared to the airway pressure waveform. If they appear similar in pressure and shape, the catheter is likely in the trachea and should be removed. If the catheter is in the esophagus, cardiac oscillations should be visible on the \( P_{es} \) waveform, indicating that the balloon is positioned in the lower third of the esophagus directly behind the heart. Some clinicians use a technique in which the catheter is intentionally inserted into the stomach, air is added to the balloon, and the catheter is then withdrawn until cardiac oscillations are observed.

The classic technique used to validate the balloon’s position requires the patient to perform static Valsalva and Müller
maneuvers with the glottis open. In patients unable to cooperate, changes in $P_{es}$ and airway pressure are assessed during a gentle push on the abdomen with the airway occluded. Airway occlusion is accomplished using the expiratory pause control on the ventilator. When changes in $P_{es}$ are equal to airway pressure, it is assumed that transmission of $P_{pl}$ to $P_{es}$ is unimpeded, and $P_{es}$ accurately reflects $P_{pl}$. A chest radiograph can also be used to validate correct positioning, but this is usually not necessary.

There are potential sources of error in the use of $P_{es}$ to estimate $P_{pl}$. It is important to appreciate that the $P_{es}$ estimates $P_{pl}$ mid-thorax. The $P_{pl}$ is more negative in the non-dependent thorax and more positive in the dependent thorax. The weight of the heart can bias the $P_{es}$ by as much as 5 cm H$_2$O. The results of Guérin and Richard suggest that referencing absolute $P_{es}$ values to those obtained at the relaxation volume of the respiratory system might improve the customization of the correction of $P_{es}$ based on the physiologic and individual context, rather than using an invariant value of 5 cm H$_2$O.

**Transpulmonary Pressure**

Transpulmonary pressure ($P_L$) is the difference between pressure measured at the mouth and esophageal (pleural) pressure. During no flow (inspiratory or expiratory pause maneuvers), $P_L$ becomes the alveolar distending pressure. In this chapter, the assumption is that $P_L$ is measured under static conditions and thus represents alveolar distending pressure. The ventilator should be set to avoid a negative $P_L$ during exhalation (contributing to cyclical opening and closing injury) and to avoid excessive $P_L$ at the end of inspiration (over-distention).

**Intra-Abdominal Pressure**

Interactions between the abdominal and thoracic compartments are important considerations in the critically ill patient, as the diaphragm links these compartments. If the diaphragm is allowed to freely shift upward into the thorax with increased abdominal
pressure, lung volume will be reduced. If lung volume is restored with PEEP, the increased abdominal pressure will result in an increase in intrathoracic pressure. On average, half of the pressure in the intra-abdominal compartment (range of 25–80%) has been noted to be present in the intrathoracic space. This wide range in transmitted pressure is likely related to the amount of PEEP that has been applied to restore lung volume. Sindi et al evaluated the correlation between esophageal and abdominal pressures in mechanically ventilated subjects undergoing laparoscopic surgery. In those subjects without respiratory disease, there was a significant but limited relationship between esophageal and abdominal pressures. They concluded that intra-abdominal pressure cannot predict $P_{es}$, but can provide complementary information useful in setting mechanical ventilation.

Intra-abdominal pressure is the steady-state pressure in the abdominal cavity. Normal intra-abdominal pressure is 5 mm Hg; it increases during inhalation with diaphragmatic contraction. Direct measurement of intraperitoneal pressure is the accepted standard for determination of intra-abdominal pressure. This is not practical, however; so the bladder method is thus most commonly used for intermittent intra-abdominal pressure measurement. The bladder is a passive structure, transmitting intra-abdominal pressure after infusion of saline volumes of 50–100 mL. Intra-abdominal pressure should be measured at the end of exhalation in the supine position, ensuring that abdominal muscle contractions are absent and that the transducer is zeroed at the mid-axillary line.

In mechanically ventilated patients, an increase in intra-abdominal pressure results in decreased $C_{RS}$ with flattening and a rightward shift of the P-V curve of the respiratory system. These changes are due to decreased $C_{CW}$, whereas $C_{L}$ remains unchanged. A strong positive correlation between intra-abdominal pressure and the lower inflection point of the P-V curve of the respiratory system has also been reported in conditions with increased intra-abdominal pressure, suggesting that intra-abdominal pressure
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might be correlated with the best PEEP in ventilated patients with ARDS and intra-abdominal hypertension. In deeply sedated patients with ARDS, the diaphragm behaves as a passive structure, and thus moves upward in the rib cage, transmits increased intra-abdominal pressure to the lower lobes of the lung, and causes compression atelectasis. Surgical abdominal decompression recruits lung volume and increases in $P_{aO_2}/F_{IO_2}$. Upright positioning increases intra-abdominal pressure and decreases $C_{RS}$, suggesting that this position might result in a deterioration of respiratory function in patients with intra-abdominal hypertension.

Transdiaphragmatic Pressure

Normally during spontaneous inspiration, $P_{pl}$ decreases and intra-abdominal pressure increases. Transdiaphragmatic pressure ($P_{di}$) represents the pressure across the diaphragm, the difference between abdominal pressure ($P_{ab}$) and $P_{pl}$: $P_{di} = P_{ab} - P_{pl}$. Abdominal pressure is measured from a catheter in the stomach (gastric pressure), and $P_{pl}$ is measured as $P_{es}$. Sharshar et al reported that $P_{di}$-driven servo ventilation was well synchronized to the subjects’ effort, delivering a pressure proportional to $P_{di}$ and reducing respiratory effort at normocapnia and hypercapnia. Although this approach has physiologic intrigue, it might not be practical for routine clinical use.

Abdominal paradox is a clinical sign of diaphragm paralysis. In this circumstance, both esophageal and gastric pressures have a negative deflection during inspiration, suggestive of diaphragmatic paralysis.

Asynchrony

Patient-ventilator asynchrony results in an airway pressure waveform that varies from breath to breath, particularly during volume control ventilation. A special form of patient-ventilator asynchrony can occur during pressure support ventilation, in which the patient actively exhales to terminate the inspiratory phase. This is seen as a pressure spike at the end of inspiration, causing
the ventilator to pressure-cycle to the expiratory phase. It is important to judge the presence of asynchrony when assessing respiratory mechanics, as this has the potential to bias assessments of respiratory mechanics such as $P_{\text{plat}}$ and stress index.

**Stress Index**

The stress index is used to assess the shape of the pressure-time curve during constant flow-volume control ventilation. A linear increase in pressure (constant compliance, stress index = 1) suggests adequate alveolar recruitment without over-distention. If compliance worsens as the lungs are inflated (progressive decrease in compliance, upward concavity, stress index > 1), this suggests over-distention, and the recommendation is to decrease the PEEP, $V_T$, or both. If compliance improves as the lungs are inflated (progressive increase in compliance, downward concavity, stress index < 1), this suggests tidal recruitment and potential for additional recruitment, and the recommendation is to increase PEEP.

The stress index is the coefficient $b$ of a power equation: $P = a \times T_1^b + c$, where the coefficient $b$ (stress index) describes the shape of the curve. Using this equation, the stress index can be determined by curve-fitting this equation during passive constant-flow inflation. One manufacturer has the stress index equation incorporated into the software of the ventilator to allow display of the stress index. Alternatively, one can examine the shape of the airway pressure waveform displayed on the ventilator. The results of a recent study using computed tomography to identify over-distention reported that injurious ventilation was associated with a $P_{\text{plat}}$ of > 25 cm H$_2$O and a stress index of > 1.05.

**BASIC PHYSICS RELATED TO MECHANICAL VENTILATION**

In simple terms the lung-ventilator unit can be thought of as a tube with a balloon on the end with the tube representing the ventilator tubing, ET tube and airways and the balloon the alveoli.
• Pressure at point B is equivalent to the alveolar pressure and is determined by the volume inflating the alveoli divided by the compliance of the alveoli plus the baseline pressure (PEEP).

• Pressure at point A (equivalent to airway pressure measured by the ventilator) is the sum of the product of flow and resistance due to the tube and the pressure at point B.

• Flow, volume and pressure are variables while resistance and compliance are constants.

• \( \text{Flow} = \frac{\text{Volume}}{\text{time}} \)

• It follows from the relationships between pressure, flow and volume that by setting one of pressure, volume or flow and the pattern in which it is delivered (which includes the time over which it is delivered) the other two become constants.

• It also follows that it is not possible to preset more than one of these variables as well as time.

Thinking of the lung-ventilator unit in terms of this simple model is also useful in aiding an understanding of the use of monitoring end-inspiratory pause pressure. In volume and flow preset modes pressure becomes a dependent variable. It is important to monitor pressure in order to minimize the risk of barotrauma. However, in this context it is alveolar pressure not airway pressure that is important. By measuring the airway pressure during an end-inspiratory pause it is possible to eliminate the component due to resistance because during an end-inspiratory pause there is no flow and thus \( P_{AW} = P_{ALV} \). In most circumstances the contribution of the resistance component to airway pressure is relatively small and constant so it is reasonable to monitor airway pressure, however in patients with high resistance (eg patients with obstructive lung disease) it is important to monitor end-inspiratory pressure. Measurement of end-inspiratory pressure may also help determine the cause of a sudden rise in airway pressure. If both are high then the problem is due to a fall in
compliance (eg endobronchial intubation, pneumothorax) while if only the airway pressure is high then the problem is due to increased resistance (eg partially blocked ETT, bronchospasm)

**Chatburn’s classification of ventilators**

- uses a framework of power source, drive mechanism, control mechanism and output
- ventilator’s functional characteristics are basically described by control mechanism and output

**Control mechanism**

- pressure, volume and flow are variables. Compliance and resistance are constants

**Variable and waveform control**

If any one of the variables and its resultant waveform can be preset the other 2 variables become dependent variables. If none can be preset the ventilator is a time-controller

- pressure control: ventilator applies a set pressure with a set waveform. Flow and volume will depend on compliance, resistance and the pressure waveform chosen

- flow control: ventilator delivers a set flow rate and pattern independent of patients respiratory mechanics and hence resultant volume is also constant. Pressure depends on flow rate and pattern, volume or inspiratory time, and respiratory system mechanics

- volume control: volume constant but specific measurement of volume distinguishes this from flow control

- time control: only inspiratory and expiratory times are controlled

**Phase variables**

- trigger variables
  - variable used to initiate inspiration
  - eg fall in airway pressure or loss of basal flow (flow-by-
trigger mode). During flow-by a continuous flow of gas is presented to the patient and is vented in toto through the expiratory tubing unless the patient makes an inspiratory effort. Machine senses any difference in this basal flow and the actual flow in the expiratory limb and this triggers a mechanical breath. The difference required depends on the sensitivity setting, usually 1-3 L/min.

- pressure may be sensed at ventilator (underestimates effort) or at Y-piece (delays sensing by transducer sited in ventilator) with no real benefit of one over other
- for given time delay flow triggering offers no advantage over pressure triggering but proper setting of flow sensitivities can reduce inspiratory work
- degree of change in variable required to trigger inspiration altered by sensitivity setting
- over sensitive settings will lead to autocyling

- limit variables
  - flow, volume or pressure can be set to remain constant or reach a maximum
  - may be same as or unrelated to variable that terminates inspiration (ie cycle variable)
  - eg preset inspiratory pressure is achieved in PSV but usually flow terminates inspiration
  - controversy as to whether flow should be volume or pressure limited
  - former has advantage of delivery of a known tidal volume but this may be at expense of high peak airway pressure
  - latter: less risk of excessive peak pressures but may be fluctuations in $V_T$ and minute ventilation due to changes in impedance

- cycle variable
  - variable used to terminate inspiration. In Europe and Australasia this is most commonly time. However in the USA it is usually volume.
- baseline variable
  • variable that is controlled during expiration
  • pressure is most practical and common

**Conditional variable**

- some ventilators capable of delivering different patterns of pressure, volume and flow depending on what conditional variables are met
  - eg in SIMV a sensed patient effort and an open spontaneous phase (“window”) will allow a spontaneous breath, otherwise a mandatory breath is delivered

**Pressure vs volume limiting**

Decelerating flow pattern, seen in pressure limited or controlled ventilation, is associated with improved gas distribution with improved ventilation-perfusion matching, and thus improved oxygenation and decreased dead space

**Ventilator settings and alarms**

**High airway pressure**

- in addition to providing alarm breath should be pressure limited and thus patient will only receive part of the preset tidal volume
  - if pressure limit is repeatedly exceeded patient should be disconnected and manually ventilated while problem diagnosed. Initial steps are to check for ETT blockage and ventilator malfunction. Other factors to consider are airway resistance, pneumothorax, endobronchial intubation
  - causes of high airway pressures include:
    • Asynchronous breathing
    • Low compliance (high peak and plateau pressures):
    • - endobronchial intubation
    • - pulmonary pathology
• pneumothorax
• - hyperinflation: dynamic, obstructed PEEP valve or expiratory port, excessive PEEP
• - ascites
• Increased system resistance (high peak pressures only):
  • - obstruction to flow in circuit, tracheal tube
  • - malplaced ETT
  • bronchospasm
  • - aspiration/secretions

- calculation of dynamic and static effective compliance may give indication of cause of increased airway pressure. Dynamic effective compliance is actually a measure of impedance as it consist of both compliance and resistance components. Dynamic effective compliance = (Peak airway pressure-PEEP)/delivered tidal volume. Static effective compliance=(Plateau pressure-PEEP)/delivered tidal volume. Delivered tidal volume=Tidal volume-ventilator compressible volume. PEEP=the higher of PEEPi and PEEP during.

  - dynamic effective compliance reduced by decreases in lung or chest wall compliance or increases in airway resistance while static compliance is not affected by resistance (assuming pressure measurement is made when there is no flow)

  - no specific airway pressure guaranteed to exclude risk of barotrauma. In fact main determinant of alveolar overdistension is end-inspiratory volume rather than pressure. However latter is easier to measure.

  Plateau pressure probably a better estimate of peak alveolar pressure than peak airway pressure. Based on animal studies and the knowledge that human lungs are maximally distended at a respiratory system recoil pressure of 35 cm H₂O maintaining plateau pressure < 35 recommended. NB if pleural pressure increases (eg due to distended abdomen) then plateau pressure will increase without an increase in alveolar pressure
**Tidal volume**

Causes of low tidal volume in pressure preset modes:

- Asynchronous breathing
- Decreased compliance
- Increased system resistance
- Inadequate preset pressure
- Gas leak

**Inspiratory flow**

\[- = \frac{\text{tidal volume}}{\text{inspiratory time}}\]

- High flow rates result in high peak airway pressures. May not be of concern provided that most of the added pressure is dissipated across the ETT. Patients may find abrupt bolus of gas uncomfortable and “fight” ventilator

- Low flows prolong inspiratory time and therefore increase mean airway pressure which may improve oxygenation but at the risk of increasing RV afterload and decreasing RV preload. Also decreases expiratory time and predisposes patient to dynamic hyperinflation.

  Patient may find flow insufficient and begin to “lead” the ventilator, sustaining inspiratory effort throughout much of the inspiratory cycle.

**Expiratory flow**

- cannot usually be set
- \[- = \frac{\text{tidal volume}}{\text{expiratory time}}\]. Latter is difference between cycle time and inspiratory time
- - principal ventilator-related determinant of dynamic hyperinflation

**VENTILATOR INDUCED LUNG INJURY**

**Oxygen toxicity**

- Probably not significant with $F_{O_2} < 0.5$
Barotrauma

Factors predisposing to barotrauma

- high airway pressures. High peak inspiratory pressures may simply be a marker of low pulmonary compliance rather than a causal factor. Incidence of barotrauma was similar in patients ventilated in CMV and HFV modes in one study of 309 patients with acute respiratory failure
- frequent positive pressure breaths
- pulmonary infection
- systemic infection
- diffuse pulmonary injury (ARDS)
- hypovolaemia

Warning signs
- PIP > 40 cmH₂O
- pulmonary interstitial emphysema on CXR. May be difficult to detect. Manifests as small parenchymal air cysts, air patterns that fail to taper toward the peripheral lung margins and haloes or crescents surrounding pulmonary vessels
- subpleural air dissection producing linear collections of air or frank air cysts
- mediastinal emphysema
- abrupt increase in PADP (8-12 mmHg)

Management of patients with pulmonary barotrauma
- pneumothoraces require drainage
- tension pneumomediastinum may cause cardiovascular collapse and require decompression. Patients may complain of chest pain and ECG changes may be present; may confuse diagnosis. Hamman’s sign (“mediastinal crunch”) present in up to 50% In infants can be achieved by insertion of a small catheter into anterior mediastinum while in adults most efficient method is to make an incision 2-3 cm cephalad to suprasternal notch and
open deep fascia beneath sternum. Tension pneumomediastinum unusual because decompression into pleural cavity and subcutaneous tissues usually occurs first.

- pneumopericardium may require immediate treatment if cardiac tamponade occurs. Treat with pericardiocentesis

- important to maintain adequate ventilation without contributing to additional morbidity and mortality. Mortality from acute respiratory failure ranges from 20-80% while barotrauma related mortality is <1%. Thus make every effort to maintain oxygenation through increased expiratory pressure (PEEP/CPAP) and increased Fio2 while reducing the number of mechanical breaths

Volutrauma

- Experiments with negative pressure ventilation have demonstrated that excessive stretch in the absence of excessive airway pressure can cause lung injury

- Trend is towards using smaller tidal volumes (7-10 ml/kg instead of 10-15 ml/kg) ARDSnet study showed tidal volumes of 4-8 ml/kg are associated with an improved outcome in patients with ALI or ARDS.

Shear stress

- Collapse and re-opening of alveoli with each tidal breath results in continual shear stress

- This is thought to play a part in ventilator induced lung injury and is the theoretical basis for use of high PEEP (above lower inflection point of static pressure volume curve).

High frequency ventilation

- def: ventilation of lungs at a frequency > 4 times normal rate

- most important difference from conventional IPPV is that it requires tidal volumes of only 1-3 ml/kg body weight to achieve normocarbia
- 3 types: high frequency positive pressure (used in anaesthesia), high frequency jet (anaesthesia and ICU) and high frequency oscillation

  Proposed advantages
  - reduced peak and mean airway pressures
  - improved CVS stability due to above
  - decreased risk of barotrauma
  - allows adequate ventilation with a disrupted airway (eg bronchopleural fistula)
  - permits mechanical ventilation during bronchoscopy
  - improves operating conditions eg in thoracic surgery
  - allows ventilation through narrow catheters and thus increases access during laryngeal and tracheal surgery
  - reduces sedation requirements when used in ITU
  - avoidance of hypoxia during tracheobronchial toilet

Disadvantages
- specialized equipment required
- dangers of high pressure gas flows
- humidification of inspired gases difficult
- tidal volumes markedly affected by changes in respiratory compliance
- monitoring of ventilation parameters difficult
- difficult to predict minute ventilation from ventilator

High frequency jet ventilation
- pulses of gas delivered at high velocity through an orifice at frequency of 10-100 Hz
  - orifice may be in a T-piece connected to a conventional ETT, in a narrow tube incorporated in wall of a special ETT or at end of fine bore catheter placed in trachea
  - in early part of inspiratory cycle jet entrains gas. Entrained
gas develops a normal flow profile which acts as a piston in trachea
  - expiration is passive
  - essential to have a free expiratory pathway to prevent barotrauma
  - entrained gas can be humidified
  - behaves like a constant pressure generator in that tidal volume is dependent on compliance
  - probably useful in barotrauma and in patients with a gas leak eg bronchopleural fistula
  - may improve haemodynamic status of patient if it leads to a reduction of airway pressure
  - ? of benefit in ARDS in combination with other methods of decreasing barotrauma

*High frequency oscillation*
  - both inspiration and expiration are active
  - piston or loud-speaker cone used to produce a sinusoidal pattern of respiration in which expiration is mirror image of inspiration
  - frequencies: 2-100 Hz
  - an auxiliary flow of gas (bias flow) crosses the oscillating gas flow to provide fresh gases and clear CO$_2$
  - behaves like a T-piece: efficiency of CO$_2$ removal is a function of bias gas flow
  - stroke volume of oscillator is less than anatomical dead space
  - mechanism of gas exchange is not clear
  - used principally in neonates with RDS. Little evidence to suggest it is superior to conventional ventilation

*Mechanisms of gas exchange*
  - direct alveolar ventilation: tidal volumes of as low as 1 ml/kg still result in direct ventilation of centrally situated alveoli
Respiratory Mechanics in the Mechanically Ventilated Patient

- enhanced diffusion: due to increased turbulence and convective mixing
- Pendelluft: adjacent lung units show asynchronous filling and emptying with slow units filling from fast units
- acoustic resonance: ? produces resonant waves which cause turbulence
- cardiogenic mixing: mixing due to mechanical interaction of heart beating against lung
- molecular diffusion

Ventilation of patients with unilateral lung disease

- in unilateral lung injury (eg following trauma, aspiration and pneumonia) ventilation may go primarily to normal lung. If high pressures and volumes are used this may result in:
  • overdistension of normal lung with resultant barotrauma and volume trauma and elevation of VD/VT
  • shunting of blood away from the good lung resulting in increased shunt

Conventional mechanical ventilation
• beware overdistension
• consider - inspiratory time and decelerating flow profile

Lateral positioning
• unaffected lung dependent
• - shunting but
• risk of spillage into good lung

Independent lung ventilation

Criteria: 1 of the following:
• PaO₂ refractory to high F̵O₂ and PEEP (PaO₂/F̵O₂ ratio <150)
• PEEP induced deterioration in oxygenation or shunt fraction
Pediatric and Neonatal Mechanical Ventilation

- Over-inflation of non-involved lung
- Significant deterioration in circulatory status in response to PEEP

**Technique**

May be synchronous or asynchronous. The latter allow each lung to be considered as an independent entity, simplifying management. Different modes, rates, pressures and volumes can be used on each side. Even different ventilators can be used. Cardiovascular problems associated with asynchronous ventilation are insignificant. PA and PAWP difficult to interpret but cardiac output and systemic pressures unchanged from pre-independent lung ventilation.

Ventilation should be titrated against blood gases and pressures/volumes obtained from each ventilator.
RESPIRATORY MONITORING

Monitoring a patient’s respiratory status usually takes place in a hospital setting and may be the primary purpose for a patient being observed or admitted to a medical setting.

The physical signs of respiratory distress may present as a patient appearing short of breath, having an increased work of breathing, use of their accessory muscles, and changes in skin color, general pallor, or partial or complete loss of consciousness.

When the initial efforts of respiratory monitoring show evidence of a patient’s inability to adequately oxygenate their blood, the patient may require mechanical ventilation.

Enhance understanding of pathophysiology

It is key to have a good understanding of patient pathophysiology in order to properly interpret medical information.

Measurement of airway pressure (Paw), flow (F) and volume (Vol) during mechanical ventilation assists in the differential diagnosis of respiratory failure. Airway occlusion technique makes possible to carefully characterize the mechanics of the lung, chest wall, and the total respiratory system. Patients with acute
respiratory distress syndrome (ARDS) can have a modified elastance due to a stiffer lung or a stiffer chest wall depending in the origin of the disease. Patients with ARDS of pulmonary origin are at greater risk of ventilator lung injury than those of non pulmonary origin.

Recording muscle activity during spontaneous breathing helps differentiate PEEPi caused by dynamic hyperinflation from that caused by expiratory muscles. If the patient's PEEPi is caused by dynamic hyperinflation, external PEEP will reduce the patient's work of breathing. If it is caused by expiratory muscles, it will add an elastic load and it will increase the operating lung volume.

During a weaning trial, esophageal pressure and flow measurement can be used to partition patient's effort into its resistive, elastic and PEEPi components. The three components are increased in patients that fail the weaning.

**Aid with Diagnosis**

Capnometry helps in detecting esophageal intubation. Monitoring flow-volume curves helps in detecting the need for endotracheal suctioning.

Presence of expiratory flow throughout expiration, without reaching zero, suggests the presence of PEEPi. With an occlusion of the expiratory port PEEPi can be measured in a patient in control ventilation.

Monitoring physiologic variables, such as the ratio of respiratory frequency to tidal volume (RR/VT) also called rapid shallow breathing index (RSBI) helps in deciding whether a patient has reasonably likelihood to tolerate discontinuation of mechanical ventilation.

**GUIDE MANAGEMENT**

**Assess the response of drugs**

Monitoring is essential with administration of therapeutic agents that can provide rapid and dramatic changes in a patient’s
condition. For example, the measurement of airway resistance helps in assessing the response to bronchodilator therapy.

**Optimize ventilator setting**

Monitoring of ventilated patients is very important in all phases of ventilation. In control-ventilation it helps to reduce the potential risk of injuring the patient with the ventilation by better knowing the patient's physiology. In assisted-ventilation it helps to set the ventilator to fulfill the patient's demand. In weaning it helps to reduce the time needed to remove the ventilator from the patient.

**Titrating Fio2**

In ventilated patients, pulse oximetry is commonly used when titrating FIO2. A reliable target of Spo2 is greater than 95%.

**Adjusting Pressure Support**

Tidal volume and respiratory rate are commonly used to set pressure-support ventilation. A reasonable level of inspiratory effort is an inspiratory pressure-time product (PTP) < 125 cmH2O.sec/minute. Pressure time product could be measured using the simultaneous recording of flow, volume and esophageal pressure. There are respiration monitors capable of measuring PTP on real time. If such a tool is not available to achieve this target, using a respiratory rate of 30 breaths/minute and tidal volume of 600mL resulted in the fewest false classifications.

**Setting PEEP**

In a patient with acute lung injury (ALI), the right level of PEEP is that which optimizes arterial oxygenation without causing O2 toxicity or ventilator-induced lung injury. Balancing the benefit of keeping the lung open (during tidal ventilation) against the risk of lung overinflation may require monitoring of the pressure-volume curve, lung morphology, and gas exchange. When loss of aeration has a focal distribution (atelectatic lower lobes coexisting with aerated upper lobes), a high level of PEEP can cause
overinflation of already aerated areas and only partial recruitment of atelectatic areas. Different strategies exist to find the level of PEEP in these patients: ARDSnet, guided by esophageal pressure, Stress Index, static airway pressure-volume curve. In such patients, some experts recommend limiting PEEP to low levels (~10cmH2O). In patients who have diffused loss of aeration PEEP can be used provided it does not cause the plateau pressure to rise above the upper inflection point.

**Assessing Patient Work of Breathing**

Work of breathing (WoB) is measured as the area of the pleural pressure – volume loop. Pleural pressure is assessed using esophageal pressure. The Campbell Diagram shows the different components of the WoB. Pressure Time Product (PTP), measures the patient respiratory effort, and has a higher correlation with oxygen consumption than WoB. During assist-control ventilation, an increase in flow can decrease work of breathing by as much as 60% in patients with acute respiratory failure. Higher flow rates can also decrease inspiratory effort in stable patients with COPD. During pressure support or assist-control ventilation, up to a third of patient effort may fail to trigger the ventilator. Such nontriggering has been shown to result from premature inspiratory efforts that are not sufficient to overcome the elastic recoil associated with dynamic hyperinflation. To trigger the ventilator, patient effort has to first generate a negative intrathoracic pressure to counterbalance the elastic recoil and then overcome the set sensitivity. The full consequences of wasted inspiratory efforts are not known. They certainly place an unnecessary burden on patients whose inspiratory muscles are already under stress. Such added stress can interfere with subsequent weaning.

**Avoid complications**

The heterogeneous lung involvement in ARDS puts some regions at risk of developing alveolar overdistension when a ventilator breath is delivered. Plateau pressure is monitored as a surrogate for end-inspiratory alveolar pressure, and may help to
minimize lung injury. Monitoring is key in early detection of hazardous situations. Mortality is four times higher when pneumothorax is not diagnosed immediately and treatment is delayed.

**Provide Alarms**

Pulse oximetry can provide an early warning of hypoxemia. An alarm on a ventilator may sound because of a change in ventilator performance or patient clinical status. An abrupt increase in peak airway pressure can arise with endotracheal obstruction or ventilator malfunction. A decrease in peak pressure can arise with a leak in the circuit. An increase in baseline airway pressure can signal malfunction of the exhalation valve.

**Assessment of Trends**

Monitoring of physiologic variables over time helps in assessing a therapeutic response. Checking for trends assist in following the course of a disease. Monitoring patient effort can guide patient management during a weaning trial. Changes in esophageal pressure over the first 9 minutes of a trial, quantified as trend index, revealed sensitivity, specificity, positive predictive value, and negative predictive value.

**PRINCIPLES OF RESPIRATORY INVESTIGATION**

Respiratory diseases are of multiple origin. Diagnosis and follow-up often requires various investigative procedures, which should be applied in an appropriate and cost-effective step-by-step evaluation.

**History**

Taking a careful clinical history is always the first diagnostic step and is an essential approach to the patient. Specific respiratory symptoms include dyspnoea, abnormal breath sounds (such as wheezing or stridor), hoarseness, cough with or without sputum production, haemoptysis, snoring and chest pain. Each may be of
different onset (acute or chronic) or severity, isolated or combined, and sometimes accompanied by general symptoms of disease such as fever, weight loss, oedema, night sweats, nocturia or daytime somnolence.

For some disease areas, additional specific questionnaires can be helpful; for example, in allergic or occupational diseases or suspected sleep apnoea.

Often, the clinical history provides – or at least suggests – the diagnosis prior to investigation.

**Physical examination**

Physical examination classically follows a sequence: inspection, palpation (feeling with the hands), percussion and auscultation (listening with a stethoscope).

Inspection may show important physical signs such as cyanosis, abnormal breathing patterns, finger clubbing, chest wall deformities, oedema, superior vena cava syndrome or Horner's syndrome.

Palpation may detect, for instance, enlarged lymph nodes, subcutaneous emphysema or points of tenderness.

Percussion may reveal areas of dullness (e.g. pleural effusion) or hyperresonance (e.g. pneumothorax) and auscultation may detect abnormal breath sounds, such as wheezes, crackles, or a pleural friction rub, signs that are characteristic of particular respiratory diseases.

The clinical history and physical examination provide the essential clues towards the possible underlying respiratory disease, guiding selection of the appropriate diagnostic investigations: laboratory tests, respiratory function tests, imaging techniques and/or biopsy procedures.

**Laboratory methods**

Besides routine laboratory blood and urine tests, several specific blood and other tests for respiratory diseases are available.
Investigations of sputum include bacteriological examination, cell differentiation, including eosinophils, and measurement of various inflammatory mediators.

Exhaled gases or exhaled breath condensates, such as carbon monoxide and exhaled nitric oxide fraction, are used as markers of inflammatory and other diseases.

**Microbiological tests**

Microbiological tests have an essential role in the investigation of infectious respiratory diseases caused by viruses, bacteria, fungi or parasites.

They include examination of expectorated (or induced) sputum and of specimens acquired by invasive biopsy techniques.

The standard bacteriological techniques of microscopy and culture are often supplemented by molecular biological techniques (PCR) for detecting the DNA (or RNA) of the organism. Testing the susceptibility to antimicrobial agents is clinically very important.

Serological tests for confirming particular infections include identification of the relevant bacteriological or virological antigens and measurement of specific antibodies, in particular the demonstration of a rise in antibody titre. Urinary antigen detection may permit the rapid diagnosis of pneumococcal and Legionella infections.

Respiratory viruses may be cultured from different materials, most easily from nose or throat swabs. Serological tests in general provide only a retrospective assessment; specific immunoglobulin M may be of greater diagnostic value.

The laboratory diagnosis of pulmonary fungal infections is usually based on isolation of the organism from cultures, histological examination and serological tests, but also on direct microscopy after special staining (*e.g.* *Pneumocystis jirovecii*).

Parasitic lung infections may be detected by microscopy of certain materials (*e.g.* stool, blood), serological tests or histological tests.
### Table: Specific laboratory tests for some respiratory diseases. *NT-proBNP: N-terminal pro-brain natriuretic peptide; LDH: lactate dehydrogenase.*

<table>
<thead>
<tr>
<th>Disease</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary embolism</td>
<td>D-dimer</td>
</tr>
<tr>
<td>Inherited emphysema</td>
<td>$\alpha_1$-antitrypsin</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>Specific genetic tests</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>Tumour marker (<em>e.g.</em> CEA, CYFRA 21-1, NSE, SCC)</td>
</tr>
<tr>
<td>Malignant mesothelioma</td>
<td>Tumour marker (mesothelin, osteopontin, fibulin)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>Procalcitonin</td>
</tr>
<tr>
<td>(Latent) tuberculosis infection</td>
<td>Tuberculin skin test, interferon-gamma release assays</td>
</tr>
<tr>
<td>Unexplained breathlessness</td>
<td>NT-proBNP (increased in heart failure)</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>Angiotensin-converting enzyme (ACE)</td>
</tr>
<tr>
<td>Extrinsic allergic alveolitis (hypersensitivity pneumonitis)</td>
<td>Specific precipitating antibodies</td>
</tr>
<tr>
<td>Asthma</td>
<td>Total and specific immunoglobulin E, skin testing with allergens</td>
</tr>
<tr>
<td>Eosinophilic diseases</td>
<td>Eosinophils</td>
</tr>
<tr>
<td>Connective tissue disorders</td>
<td>Immunological tests such as rheumatoid factor</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>Total protein, LDH, glucose, cholesterol and others in pleural fluid</td>
</tr>
</tbody>
</table>

### Histological and cytological examination

Histology and cytology play a central role in the diagnosis of many malignant and benign respiratory diseases, including infections. Apart from expectorated sputum, which can be examined cytologically, the specimens are acquired using various biopsy techniques and are sent for histological and/or cytological
evaluation. Conventional histopathological techniques are often supplemented by immunohistochemistry using specific markers for the differentiation of several neoplasms, such as small cell neuroendocrine carcinoma and malignant lymphoma. In addition, results from molecular diagnostic tests may have important therapeutic ('targeted' treatment) as well as prognostic implications in certain types of nonsmall cell lung cancers (e.g. if mutations of the epidermal growth factor receptor (EGFR) are present).

Cytopathological examination is used mainly in the diagnosis of malignancies (e.g. malignant effusion). In bronchoalveolar lavage fluid, it may be helpful in the diagnosis of some interstitial lung diseases, such as extrinsic allergic alveolitis (hypersensitivity pneumonitis), eosinophilic pneumonia, alveolar proteinosis or asbestosis.

Ultimately, autopsy examination of the lung may provide important information regarding the underlying disease, but it is rarely performed nowadays.

THERMISTOR RESPIRATORY MONITOR

Thermistor Measurements

The resistance over the thermistor drops when its surrounding temperature increases, and goes back down when the temperature decreases. The voltage also, accordingly drops when a person exhales and rises when a person inhales. We use an operational amplifier to make the changes in temperature more apparent. The output of the amplifier is read into the microcontroller's ADC channel 0.

Voltage Measurements

Under battery operation, our device takes a voltage sample across the battery about every minute. Since our device uses a 9V battery, a voltage divider is used to drop the voltage so that it is about 2.2V at PINA1 (ADC channel 1).
Power

Our device can be powered through either a standard AC power supply or a single 9V battery.

Turn On Display

To conserve power, the user must hold down a button to turn on the display to read the respiration rate. This prevents the user from leaving the display on by mistake and draining the battery.

Output Sound

There are two different alarms for our device generated by a piezoelectric speaker. The first is higher in pitch and alarms if the patient is not breathing. The second is a signal that the device is running on low battery. While the first alarm is a continuous sound, the low-battery alert is a one-second long tone.

Respiration Rate Display

Breathing rate is measured and displayed in breaths/min on an LCD. This allows whoever is monitoring the patient to see if the patient is breathing too fast or too slowly.

Measurement

This task does the actual calculation of the respiration rate using samples from ADC0.

DESIGN DECISIONS

Microcontroller

When choosing a microcontroller for this project, we first wanted to find the smallest microcontroller possible so that it could be mounted right onto the device's mask. However, when identifying how many I/O ports and ADC channels would be necessary for our project, we realized that the AtMega1284p microcontroller that we had been using all semester would be ideal.
Thermistor

During the initial stages of our project design we experimented with several thermistors and their placement on the device. Since a drastic temperature difference is not produced when a human breathes, we needed the smallest, and therefore most sensitive thermistor we could find. Larger thermistors we experimented with either could not detect a "breath" or had a very slow response time. We also thought a mask around the patient’s nose and mouth would be the least intrusive placement of the thermistor.

Display

Because we wanted to design our device to be low-powered, choosing the right display for the respiratory rate was a concern. Originally, we planned to use two 7-segment displays which turned on when the user pressed a button. However, we decided to use an LCD screen for a nicer display. In order to reduce power usage, the LCD only receives power when the user presses the display button, which reduces the load on the battery.

Standards

As a medical device, this respiratory monitor must meet regulatory requirements outlined by governments. This includes meeting HIPPA standards which protects individuals’ medical records and other personal health information, including respiration rate. However, since we are not planning to store this information, this regulation should not be an issue. Before it can be sold commercially in the United States, the device would also need FDA approval.
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Pediatric and Neonatal Mechanical Ventilation
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The introduction of mechanical ventilation in the 1960s was one of the major new interventions in neonatology, which provided lifesaving support for infants with respiratory failure. Along with other technologic advancements, such as the administration of antepartum corticosteroids and replacement surfactant therapy, mechanical ventilation has led to improved neonatal survival, especially for preterm infants born less than 30 weeks gestation with immature lung function.

Mechanical ventilation is the process of supporting respiration by manual or mechanical means. When normal breathing is inefficient or has stopped, mechanical ventilation is life-saving and should be applied at once. The ventilator increases the patient's ventilation by inflating the lungs with oxygen or a mixture of air and oxygen. Ventilators play an important role in the anaesthetic management of patients, as well as in the treatment of patients in the ICU. However, there are differences between the anaesthetic ventilators and the ventilators in ICU. The main indication for mechanical ventilation is difficulty in ventilation and/or oxygenation of the patient because of any respiratory or other disease. The aims of mechanical ventilation are to supply adequate oxygen to patients with a limited vital capacity, to treat ventilatory failure, to reduce dyspnoea and to facilitate rest of fatigued breathing muscles. Depression of the central nervous system function is a prerequisite for mechanical ventilation.

The development of the respiratory system in the fetus begins at about 4 weeks and continues into childhood. Ectodermal tissue in the anterior portion of the head region invaginates posteriorly, forming olfactory pits, which ultimately fuse with endodermal tissue.
of the early pharynx. At about this same time, an protrusion of endodermal tissue extends anteriorly from the foregut, producing a lung bud, which continues to elongate until it forms the laryngotraceal bud. The proximal portion of this structure will mature into the trachea, whereas the bulbous end will branch to form two bronchial buds. These buds then branch repeatedly, so that at about week 16, all major airway structures are present. Development progresses after week 16 as respiratory bronchioles and alveolar ducts form, and extensive vascularization occurs.

Respiratory mechanics refers to the expression of lung function through measures of pressure and flow. From these measurements, a variety of derived indices can be determined, such as volume, compliance, resistance, and work of breathing. Plateau pressure is a measure of end-inspiratory distending pressure. It has become increasingly appreciated that end-inspiratory transpulmonary pressure (stress) might be a better indicator of the potential for lung injury than plateau pressure alone. This has resulted in a resurgence of interest in the use of esophageal manometry in mechanically ventilated patients. End-expiratory transpulmonary pressure might also be useful to guide the setting of PEEP to counterbalance the collapsing effects of the chest wall. The shape of the pressure-time curve might also be useful to guide the setting of PEEP (stress index). This has focused interest in the roles of stress and strain to assess the potential for lung injury during mechanical ventilation. This book covers both basic and advanced respiratory mechanics during mechanical ventilation.

All the matter is just compiled and edited in nature. Taken from the various sources which are in public domain.

This book is focus on the effective delivery of respiratory support to children, infants and newborns.

—Editor
ABOUT THE BOOK

The introduction of mechanical ventilation in the 1960s was one of the major new interventions in neonatology, which provided lifesaving support for infants with respiratory failure. Along with other technologic advancements, such as the administration of antepartum corticosteroids and replacement surfactant therapy, mechanical ventilation has led to improved neonatal survival, especially for preterm infants born less than 30 weeks gestation with immature lung function. Respiratory disease in its various forms remains the most common cause of pediatric and neonatal morbidity and mortality. One of the most common reasons for admission to pediatric or neonatal intensive care units is the need for ventilatory support for acute or impending respiratory failure. The major challenge for these units is to deal with a very heterogeneous population of patients who are characterized by enormous differences in age and size and marked developmental changes in organ physiology during growth. In particular, the pediatric intensive care unit population is characterized by a wide variety of rare and unique medical problems that make large clinical trials, even on general topics such as ventilator support, very difficult to conduct. This book is focus on the effective delivery of respiratory support to children, infants and newborns.

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