Mechanical Ventilation from Pathophysiology to Clinical Evidence

Giacomo Bellani
Editor

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Foreword

Writing a few words of introduction for this new book *Mechanical Ventilation: from Pathophysiology to Clinical Evidence* is an opportunity to stress the fact that Mechanical Ventilation still is the most widely applied life support technique in the care of the Critically Ill Patient.

Millions of people, every year, owe indeed their survival to Mechanical Ventilation.

In 1952, thanks to the physiological approach of Dr. Bjorn A Ibsen, it warranted the necessary ventilatory support to children affected by poliomyelitis. From then on, it has developed from a simple technique to a sophisticated clinical science; as such it requires a solid knowledge of pathophysiological principles, a familiarity with the technology and the devices involved, and a deep clinical background, extending well beyond the respiratory system.

Starting with the Polio epidemic in Copenhagen, through the most recent H1N1 influenza and the latest COVID-19 pandemic, Mechanical Ventilation has proven the single most important vital support in epidemic situation, and a fundamental backbone of the critical care approach.

This book endeavors to cover systematically the vast clinical science of Mechanical Ventilation, from Pathophysiology to Clinical Evidence, as its title says. It addresses mainly the field of Critical Care, moving from the basic technical background to pathophysiological monitoring, up to the real life of clinical scenarios.

This rather original approach provides an effective guide to the topic, providing a critical update of the science of Mechanical Ventilation.

A most impressive team of authors generated this book, bound to become a most important reference for anyone interested in this discipline.

I congratulate the Editor, Giacomo Bellani, and all the authors, for their achievement.

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Preface

I was asked many times what brought me to the decision of realizing a book on Mechanical Ventilation. And the answer, such as the idea underpinning this book, is rather simple: I am strongly convinced that, in clinical practice, while guidelines are necessary, and protocols might be useful, mechanical ventilation cannot be managed optimally unless clinicians have proper knowledge and understanding of physiology (which during disease becomes "pathophysiology") of the respiratory system–ventilator complex. From pathophysiology stem the concepts that are tested in clinical trials and are incorporated in guidelines.

Moreover, several papers open with a sentence that sounds like "Mechanical Ventilation is a life-saving treatment for acute respiratory failure….." And this is certainly the case. However, what I find almost unique to mechanical ventilation is that it gives a unique opportunity to understand the disease of our patients and to monitor in real time the response to clinical interventions. Just by looking at a waveform and measuring a few parameters, we may judge if increasing PEEP led to overdistension, if a bronchodilator we just introduced is working or not, if patient is receiving too much assistance from the ventilator or too little, if patients fail weaning due to muscle weakness, only to quote a few examples. Hence, Mechanical Ventilation is, indeed, also a diagnostic tool (often in real time). This is especially important in an era of personalized medicine: guidelines and protocols—while undoubtedly useful—will never have the granularity nor will be able to integrate all the complex information required to treat a specific patient. Optimizing the patient–ventilator interaction to achieve the best possible outcomes is personalized medicine at the bedside. Again, only understanding pathophysiology will be a crucial tool to achieve this goal.

I must also say that, overall, the book definitely exceeds my expectations. I have had the privilege, over the years, to meet many colleagues who are real experts on the topics. By reading their papers and listening to their talks, it is clear that their knowledge comes also from everyday practice and experience. I was proud and honored when they accepted to collaborate in this project, and they have all provided extremely high-quality chapters. It is important to know that I asked the authors to limit the number of references: rather than a fully exhaustive literature overview, I felt more useful to point the readers toward the resources who the authors judged more useful. Hence if some relevant reference is missing, no blame on the authors.

I sincerely hope that this book will help our (especially younger) colleagues not simply to "learn" and, most importantly, to "understand" Mechanical Ventilation but also to be "captured" by it, so to be in the position of developing and testing novel ideas and/or become teacher to others.

Monza, Italy Giacomo Bellani

Contents

Part I

Techniques

Basic Physiology of Respiratory System: Gas Exchange and Respiratory Mechanics

1

Khoi Do and Guido Musch

1.1 Gas Exchange

Gas exchange is the process by which atmospheric oxygen (O_2) is transferred from the alveolar gas into the bloodstream and carbon dioxide (CO_2) from the bloodstream into the alveolar gas phase. CO_2 is then eliminated into the atmosphere by ventilation. Gas exchange occurs at the level of the transitional and respiratory zones of the respiratory system, which are areas of the lung lined by alveoli. Alveoli are tiny air sacs encased in capillary beds (Fig. 1.1). The proximity between air and blood in the alveoli creates an optimal environment for gas exchange. O_2 and CO_2 are brought to the site of gas exchange by ventilation and perfusion, respectively, and their transfer across the air-blood interface (i.e., alveolo-capillary membrane) is driven by simple diffusion down partial pressure gradients [1]. In this section, we discuss the individual components of gas exchange: delivery of O_2, removal of CO_2, ventilation-to-perfusion matching, and gas diffusion.

Atmospheric oxygen is delivered to the alveoli by ventilation. The primary determinant of the amount of O_2 delivered to the alveoli is the fraction of inspired O_2. This is best appreciated through the alveolar gas equation where P_AO_2 = partial pressure of alveolar O_2, P_{atm} = atmospheric barometric pressure, P_{H_2O} = partial pressure of water vapor at body temperature, F_IO_2 = fraction of inspired O_2, P_ACO_2 = partial pressure of alveolar CO_2, and R = ratio of CO_2 entering to O_2 leaving alveolar gas (i.e., respiratory quotient) [1, 2].

$$P_AO_2 = \left[\left(P_{atm} - P_{H_2O}\right) \times F_IO_2\right] - \left(\frac{P_ACO_2}{R}\right)$$

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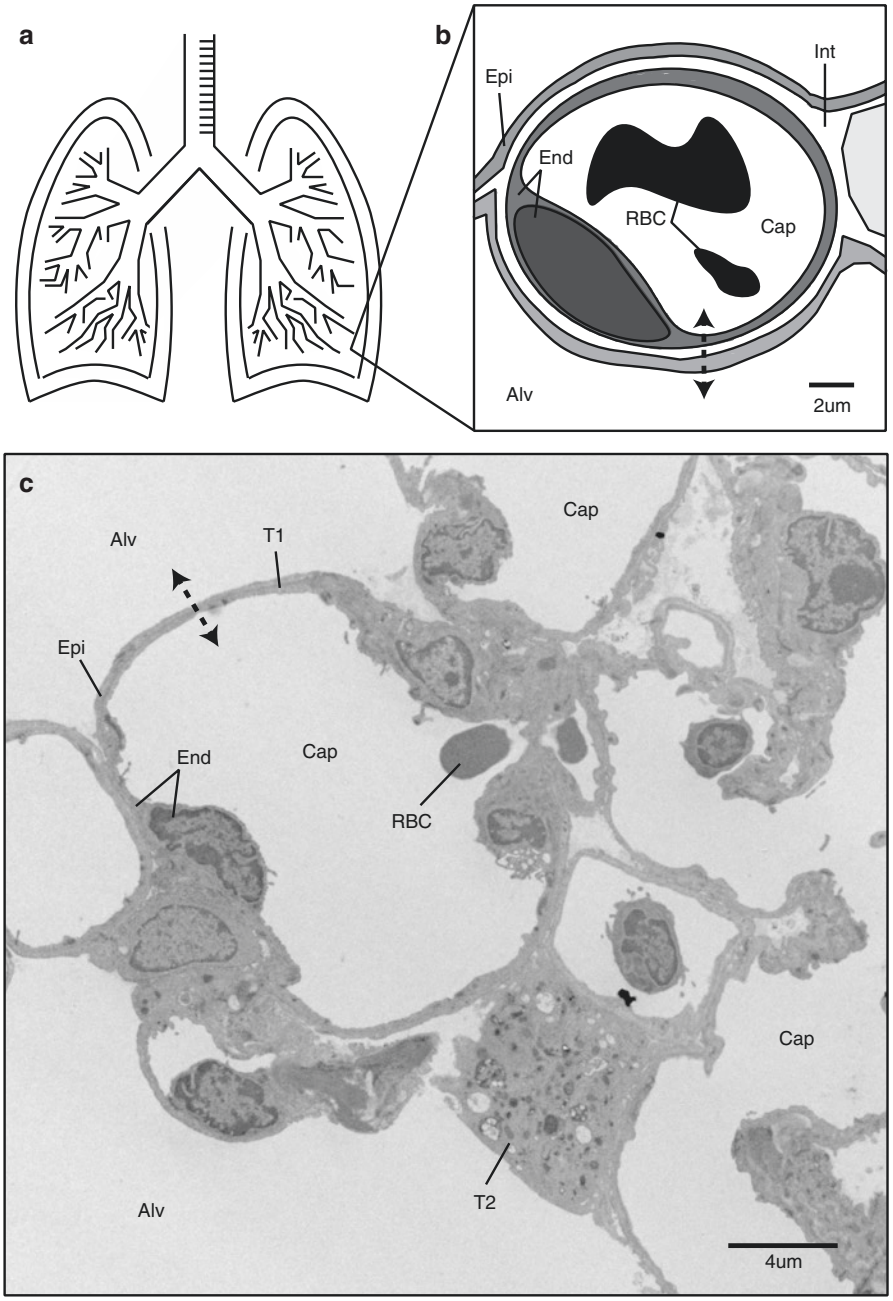

Fig. 1.1 (**a**) Gas exchange occurs at the distal airways, also known as the transitional and respiratory zones. Illustrated (**b**) and electron microgram (**c**) cross sections of pulmonary capillaries (Cap) embedded within alveoli (Alv). The double-sided arrow indicates the diffusion pathway of gases across the air-blood interface. This interface, also referred to as alveolo-capillary membrane, consists of alveolar epithelium (Epi) juxtaposed to capillary endothelium (End) through the respective basement membranes. Type I (T1) and type II (T2) pneumocytes can be visualized on the electron microgram

Once O_2 arrives in the alveoli, the primary force driving it into the blood is the partial pressure gradient across the alveolo-capillary membrane, which is the difference between P_AO_2 and the partial pressure of O_2 in returning mixed venous blood. As seen in the equation, P_AO_2 comprises of the difference between the partial pressure of inspired oxygen within the airway ($[(P_{atm} - P_{H_2O}) \times F_IO_2]$) and the drop in the partial pressure of O_2 due to diffusion of O_2 into the capillary blood (P_ACO_2/R). Apart from F_IO_2, the other variables are relatively fixed. By increasing F_IO_2, P_AO_2 is also increased, increasing the partial pressure gradient between alveolar O_2 and mixed venous O_2, increasing the driving force for O_2 diffusion from the alveoli into the blood.

Carbon dioxide is a natural byproduct of cellular metabolism and is carried by the venous system to the pulmonary capillary bed where it diffuses into the alveoli and is excreted into the atmosphere. Unlike oxygen delivery, the elimination of carbon dioxide is determined primarily by ventilation. The mean alveolar partial pressure of CO_2 is determined by the following equation where F_ACO_2 = fraction of alveolar CO_2, $\dot{V}CO_2$ = rate of CO_2 production by the tissues, $\dot{V}_E$ = minute ventilation, and $\dot{V}_d$ = dead space ventilation [1, 2].

$$F_ACO_2 = \frac{\dot{V}CO_2}{\dot{V}_E - \dot{V}_d}$$

The expression ($\dot{V}_E - \dot{V}_d$) represents alveolar ventilation rate, or the volume of inspired air that participates in gas exchange. In this equation, $\dot{V}CO_2$ is a function of metabolic processes and $\dot{V}_d$ is anatomically set whereas $\dot{V}_E$ is acutely modifiable. Minute ventilation is the product of tidal volume and respiratory rate. By modifying either of these variables, the amount of CO_2 eliminated can be increased or decreased. For example, if tidal volume or respiratory rate increases, F_ACO_2 decreases, increasing the partial pressure gradient between the mixed venous blood and the alveoli, driving more CO_2 into the alveoli.

As discussed, O_2 is delivered to the site of gas exchange by ventilation and removed by perfusion, whereas CO_2 is delivered by perfusion and removed by ventilation. For optimal gas exchange, ventilation ($\dot{V}$) and perfusion ($\dot{Q}$) must match. The ideal $\dot{V}/\dot{Q}$ ratio is 1. This value is achieved in the middle portions of the lung in erect subjects. However, up the lung from the base to the apex, $\dot{V}/\dot{Q}$ ranges from 0.3 to 2.1 [3]. The value of $\dot{V}/\dot{Q}$ affects the value of P_AO_2 and P_ACO_2 and thus gas exchange (Fig. 1.2). If a region of lung is perfused but not aerated, for example because it is filled with edema fluid, $\dot{V}/\dot{Q}$ is zero and O_2 cannot enter nor CO_2 leave. As a result, the venous blood is shunted through the pulmonary circulation of that region, without participating in gas exchange and thus retains O_2 and CO_2 partial pressures of mixed venous blood. Physiologically, this shunting of deoxygenated, hypercarbic blood can severely decrease O_2 saturation and content in the arterial blood, causing an increase in the alveolo-arterial O_2 (A-a) gradient. The ensuing hypoxemia is refractory to an increase in FiO2. Shunting also reduces the efficiency of CO_2 excretion. If the subject is able to enact a compensatory rise in minute ventilation, shunting will not lead to hypercarbia. If instead minute ventilation is fixed, as is the case for example of a patient on controlled mechanical ventilation, shunting will lead also to CO_2 retention, in addition to hypoxemia. On the other hand, if a

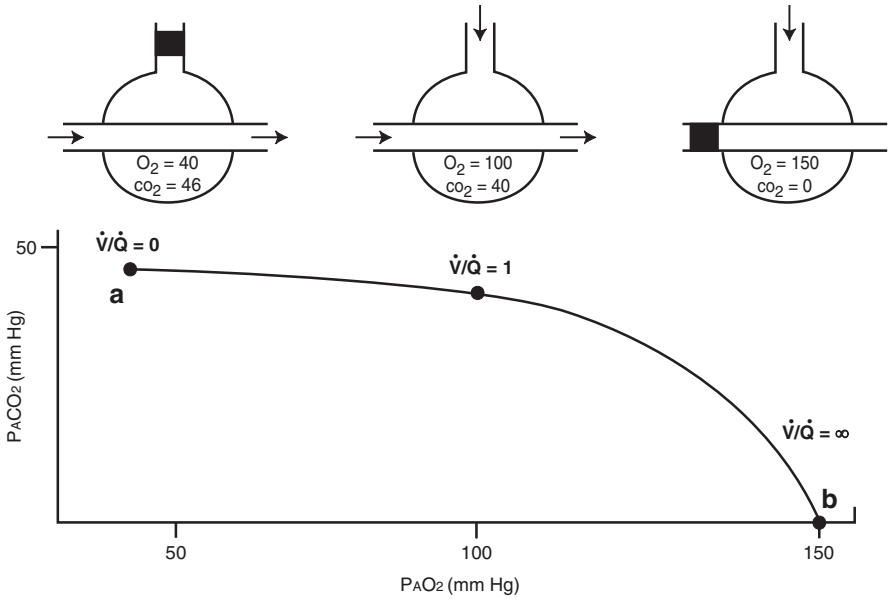

Fig. 1.2 O_2-CO_2 diagram illustrating the relationship between ventilation-perfusion ratio (V/Q) and alveolar oxygen (P_AO_2) and carbon dioxide (P_ACO_2) partial pressures in a lung unit. Lung units comprise of alveoli and pulmonary capillaries. Arrows denote airflow and blood flow. The curve represents the P_AO_2 and P_ACO_2 of all V/Q values between 0 and ∞. Point (a) illustrates shunting and point (b) illustrates dead space. (reproduced from reference [1] with permission)

region of lung is not perfused, for example because of a pulmonary embolus, but is ventilated, V/Q mathematically tends to infinity and such region functionally becomes dead space ventilation, with the partial pressures of both O_2 and CO_2 matching those of the conducting airways. Physiologically, extremely high V/Q alveoli increase alveolar dead space and dead space ventilation. The mismatch of V/Q can drastically affect the alveolar concentrations of both gases in different ways and have significant physiological effects on gas exchange.

The final component of gas exchange is diffusion of O_2 and CO_2 molecules between alveoli and pulmonary capillary blood. The gas molecules traverse the thin epithelial-endothelial membrane of the air-blood interface in opposite directions down their respective partial pressure gradients. The rate of gas movement (V) is primarily determined by Fick's law of diffusion where A = membrane surface area, ΔP = difference in gas partial pressure across the interface, and D = distance that the molecules must travel [1, 2].

$$\dot{V} = \frac{A(\Delta P)}{D}$$

Oxygen diffuses down a gradient from mean alveolar partial pressure (100 mmHg at room air) to a mixed venous partial pressure of 40 mmHg. Carbon dioxide diffuses from a mixed venous partial pressure of 46 mmHg to a mean alveolar partial pressure of 40 mmHg. The remaining parameters of Fick's equation are optimized

by the body to maximize diffusion. The air-blood interface is extremely thin (0.2–0.3 μm) with an enormous surface area of 70–80 m^2. These optimized conditions allow for rapid diffusion of gases even at higher blood flow. In fact, diffusing gases take only one-third of the 0.75-s pulmonary capillary transit time to equilibrate [2].

1.2 Respiratory Mechanics

Respiratory mechanics refers to lung function as described by relationships between pressure, gas flow, and volumes. Understanding it requires comprehension of the gross anatomy of the respiratory system. The respiratory system consists of the airway, lung, and chest wall. The chest wall comprises the rib cage and the diaphragm. Between the lungs and the chest wall is a virtual space, the intrapleural space. The pleural fluid in the intrapleural space serves two roles: lubrication of the adjacent, sliding pleural surfaces, and adhesion of the lung to the chest wall.

Within the respiratory system is the presence of opposing static forces, exhibited by the lung and chest wall which can be schematically viewed as two springs in parallel with one spring compressed below its resting volume (the chest wall) and one spring elongated above its resting volume (the lung) (Fig. 1.3) [4]. The lung naturally pulls inwards while the chest wall pulls outwards. With pleural fluid

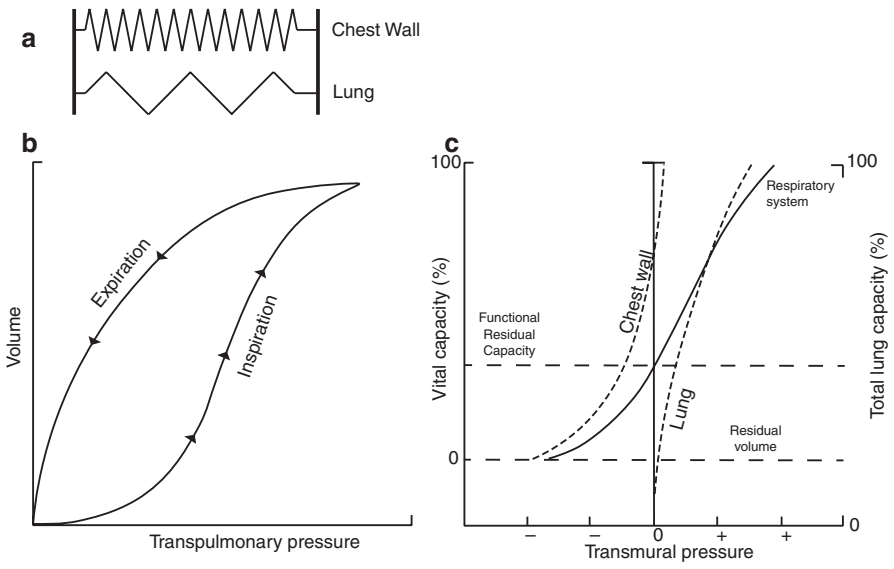

Fig. 1.3 (**a**) Parallel springs representing opposing static forces of the chest wall and lung. (**b**) Pressure-volume curve of air-filled lung during inspiration and expiration. (**c**) Pressure-volume curve of lung, chest wall, and respiratory system. The curve of the respiratory system is the sum of the lung and chest wall curves. The resting or equilibrium volume is the point where each curve intersects the *Y*-axis. The respiratory system is at equilibrium at the functional residual capacity (FRC). Panels (**b**) and (**c**) are reproduced from reference [1] with permission

adhering the two components, these opposing forces contribute to the structural integrity of the respiratory system and are essential for proper ventilation.

The lung's inward directed force results from two factors: the elastic recoil of lung tissue and surface tension. Elastic recoil refers to the tendency of an object to resume its natural shape after being stretched or compressed, and can be measured by its elastance (i.e., the pressure needed to provoke a unit volume change, $\Delta P/\Delta V$). The reciprocal of elastance is compliance, which refers to the property of an object to deform when subjected to an applied force, i.e., the change in volume per unit change in pressure ($\Delta V/\Delta P$). The compliance of the lung varies at different volumes. Lung tissue is generally more compliant and distensible at lower volumes and becomes stiffer and less compliant with increased volume [4]. This phenomenon can be appreciated by the pressure-volume curve of the air-filled lung on inspiration and expiration (Fig. 1.3). Notice the relatively steep slope of both curves at low to medium pressures and flattening of the curves near the upper limit of pressure values. The reduced compliance or increased elastic recoil at higher volumes is due to elastin and collagen fibers within the lung tissue. This increased elastic recoil at higher volumes is an intrinsic property of the lung and is one of the forces contributing to its inward pull.

The second factor that contributes to the inward pull of the lung is surface tension. Surface tension is the attractive force between adjacent liquid or air molecules. The surface of the alveoli is coated by a layer of fluid that is in contact with air, continuous with the airways, forming an air-liquid interface. Because the liquid molecules have greater attraction relative to the air molecules, they pack tighter together through cohesive forces which generate a collapsing pressure that tends to decrease the volume of the alveolus. The summation of these collapsing pressures across alveoli, as a result, pulls the lung inward [1].

A significant problem that surface tension poses is that it decreases the compliance of the lung especially at lower volumes, requiring increased effort to initiate inspiration. This phenomenon can be observed in the pressure-volume curve of the lung on inspiration (Fig. 1.3). Note the initial relatively flat part of the curve, which corresponds to reduced compliance. The lung must overcome surface tension to expand. To lessen this initial load, type II pneumocytes in the lower respiratory tract produce surfactant, a phospholipid that alleviates the restrictive effect of surface tension at low lung volumes, increasing lung compliance during initial inspiration without jeopardizing the lung's elastic recoil. Surfactant also acts as an alveolar "stabilizer" by maintaining alveolar collapsing pressure (P_c) within an optimal range [5]. It does this by regulating the surface tension (T) as defined by the law of Laplace for spheres where P_c = collapsing pressure, T = surface tension, and r = radius [1, 4].

$$P_c = \frac{2T}{r}$$

By Laplace's law, reducing the radius of an alveolus will increase the collapsing pressure. This will prompt further reduction of alveolar radius and hence trigger a

positive feed-forward mechanism that would eventually lead to alveolar collapse. In fact, alveoli across the lung have varying radii (0.1–0.25 mm). In the absence of surfactant, the smaller alveoli would tend to collapse, transferring the collapsed volume to adjacent alveoli, which would instead increase in size, reducing their P_c and thus tending to enlarge even more. In theory, this could dramatically skew the range of alveolar volumes throughout the lung. Surfactant prevents this by maintaining a surface tension that discourages both alveolar collapse and hyperexpansion. It does so because when alveoli shrink, the molecules of surfactant get packed more closely together, thus repelling each other and lowering T. When instead alveoli expand, the molecules of surfactant become more rarefied in the liquid lining of the alveoli. This reduces their tensioactive power, leading to an increase in T which opposes the expansion by restoring higher P_c. Consequently, the absence of surfactant can result in stiff, heterogeneously aerated lungs with atelectatic areas interspersed with hyperexpanded areas [6].

Contrasting the inward pull of the lung is the natural tendency of the chest wall to pull outward. Relative to the lung, the chest wall has a larger resting volume. The main factor responsible for this is the natural outward elastic recoil of the chest wall, mainly due to cartilage, bone, and muscle.

The inward pull of the lung and the outward pull of the chest wall adhered together by the pleural fluid create a dynamic relationship between opposing forces. The point where these opposing forces balance each other is the point where the system is in equilibrium. As the system deviates from equilibrium, it is pulled back into equilibrium by a corrective force. This is thus a typical case of stable equilibrium.

The equilibrium between the inward pull of the lungs and the outward pull of the chest wall is best illustrated through the pressure-volume curves of the relaxed lung, chest wall, and respiratory system (Fig. 1.3) [1]. The curves show the transmural pressure across each of the 3 structures at volumes ranging from residual volume (RV) to total lung capacity (TLC). The curve representing the lung shows that even at residual volume the transpulmonary pressure (i.e., alveolar pressure minus pleural pressure) is positive, indicating that the lungs maintain an inward elastic recoil. The chest wall curve instead shows that the transthoracic pressure remains negative (i.e., the pleural pressure is lower than atmospheric pressure) up to volumes that approach TLC. The curve representing the respiratory system is a summation of the curves representing the lung and the chest wall, and is generated by calculating the sum of the transpulmonary pressure and the transthoracic pressure at various volumes. The point where the respiratory system curve crosses the y-axis, demarked as the functional residual capacity (FRC), is the point whereby the system reaches its equilibrium volume and the inward recoil of the lung is balanced by the outward recoil of the chest wall. At higher volumes, there is positive intrapulmonary (i.e., alveolar) pressure which forms a gradient that pushes air out, moving the curve back to FRC. The opposite is true for volumes below FRC.

Ventilation occurs when the respiratory system expands above or deflates below, and then returns, to its resting or equilibrium volume. The cerebral cortex and the midbrain regulate inspiration via the medullary respiratory center's dorsal and

ventral respiratory groups (DRG/VRG). Inspiration is initiated by activation of the diaphragm and external intercostal muscles through the phrenic and intercostal nerves, respectively. The diaphragm contracts and depresses inferiorly while the external intercostals pull the ribs and sternum up and outwards, increasing thoracic cavity volume. The increase in thoracic volume decreases the intrapleural pressure and consequently the intrapulmonary (i.e., alveolar) pressure (Fig. 1.4). This causes a negative intrapulmonary pressure relative to the atmospheric pressure, producing a pressure gradient which promotes the inward movement of gas until the intrapulmonary pressure equalizes with the atmospheric pressure. Forced inspiration involves recruitment of additional muscles (i.e., sternocleidomastoid, scalene, and pectoralis minor) which cause a larger chest expansion and a larger pressure gradient, thus increasing the flow and volume of inward bound air [1].

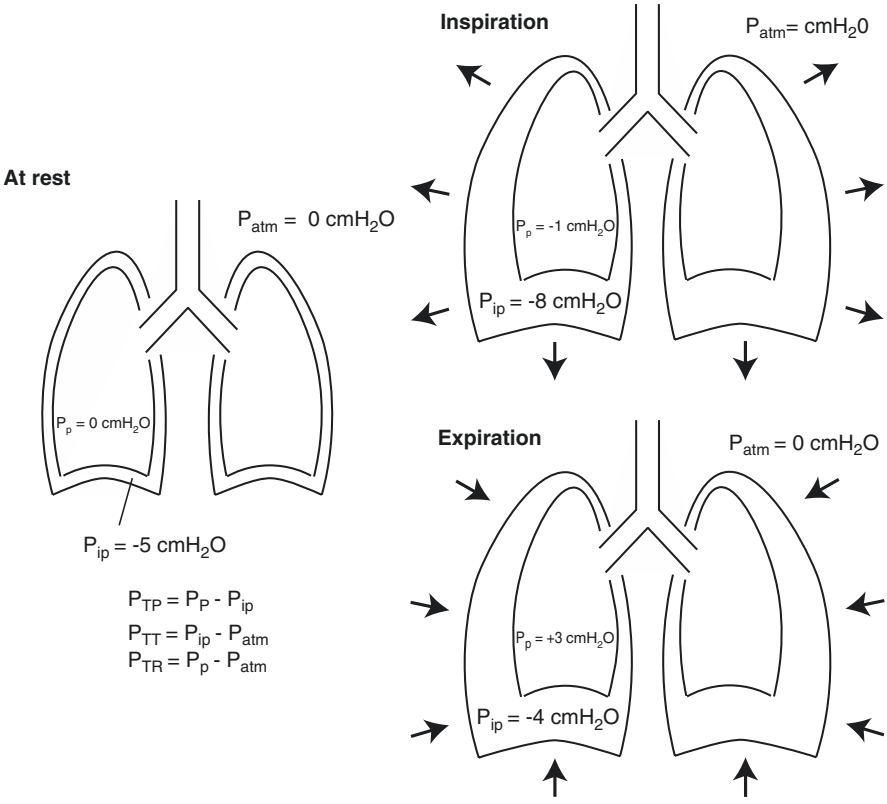

Fig. 1.4 Respiratory mechanics during inspiration and expiration. Contraction of the inspiratory muscles causes pressure changes that result in inward bound gas flow and hence increase in lung volume. When inspiration ceases, the elastic recoil of the respiratory system reverses the gradient between intrapulmonary and atmospheric pressure, resulting in expiratory airflow. P_p intrapulmonary pressure, P_{ip} intrapleural pressure, P_{atm} atmospheric barometric pressure, P_{TP} transpulmonary pressure, P_{TT} transthoracic pressure, P_{TR} transrespiratory pressure

Expiration is usually a passive process, requiring no muscle activity and solely based on the elastic recoil of the lung. At the end of inspiration, stretch receptors within the thoracic cavity inhibit the VRG, inhibiting further action potentials to the diaphragm and external intercostals. The respiratory system's elastic recoil then causes the intrapulmonary pressure to become positive relative to the pressure in the upper airways and atmosphere, creating a pressure gradient that promotes outward flow of air (Fig. 1.4). Forced expiration entails activation of the abdominal muscles (i.e., external/internal oblique, transverse abdominis, and rectus abdominis) and the internal intercostals, resulting in a larger increase in intrapulmonary pressure than by elastic recoil alone. This added force increases the flow of air and the expired volume [1].

Both inspiration and expiration involve the flow of gas through the airways. A first-approximation model to describe this process is Poiseuille's laminar flow model of either liquid or gas flowing through a tube [6]. This model is based on the equation below where Q = liquid or gas flow, ΔP = pressure gradient at the two ends of the tube, and R = resistance.

$$\dot{Q} = \frac{\Delta P}{R}$$

From this equation we can derive specific relationships, such as that greater pressure gradients generate greater flow for a given resistance or that greater resistance decreases flow. Resistance for laminar flow follows the equation below where η is viscosity, l is tube length, and r is the radius of the tube.

$$R = \frac{8nl}{\pi r^4}$$

Thus, the radius of a tube can significantly affect the resistance, and by extension the flow through a tube, because r appears in the above formula to the fourth power. The conducting airways (bronchi) have large diameters. The smaller bronchioles have tiny radii but their total cross-section is massive. Consequently, the major point of pressure drop along the bronchial tree is the medium-sized bronchi. At the respiratory bronchioles, gas flow stops, and diffusion is the predominant process driving respiratory gases across the alveolar membrane.

The factors that affect airway resistance follow the principles established by Poiseuille's law. The first factor is lung volume. Larger lung volumes decrease resistance while smaller lung volumes increase resistance. As the lung expands, the airways are dilated due to the radial traction of the surrounding lung tissue. At very low lung volumes, airways may close completely, especially in the lower part of the lung. The body also utilizes the autonomic nervous system to regulate airway diameter through smooth muscle tone. Sympathetic activity causes bronchodilation through β2 adrenergic receptors while parasympathetic activity causes bronchoconstriction through muscarinic receptors. Finally, the viscosity of the inhaled gas can affect the resistance, with higher viscosity causing higher resistance and lower flow rates [1].

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A Short History of Mechanical Ventilation

2

Philippe R. Bauer

2.1 Respiration, Circulation, and Their Interaction

The importance of the respiratory system was already invoked in the Bible as the breath of life: "And the Lord God formed man of the dust of the ground, and breathed into his nostrils the breath of life" (Genesis 2:7) [1]. The discoveries that led the mechanical ventilation span over two centuries (Fig. 2.1). The discovery of the respiratory system itself is attributed to Aelius Galenus or Galen, a Greek physician, in the second century AD, for his anatomical work entitled "*De usu partium corporis humani"* on the trachea and lungs in animals, the first reported mechanical insufflation of the lungs and the interaction between respiration and circulation. Leonardo da Vinci demonstrated that air enters the lungs through the bellows action of the chest wall. The first application of positive pressure ventilation by inserting a tube into the trachea of animals is attributed to Andreas Vesalius in 1543 in his anatomical work entitled "*De Humani Corporis Fabrica*" [2]. In 1667, Robert Hook reproduced Vesalius' experiment successfully [1]. The thought process was that air going into the lungs cools the heart and blood going into the arteries cools the body [1].

2.2 Oxygen, Combustion, Metabolism, Homeostasis

Although suspected since 200 BC in various experiments on air combustion—including those by Leonardo da Vinci—, oxygen was discovered in 1774 simultaneously by Carl Wilhelm Scheele and Joseph Priestley, and Antoine Lavoisier demonstrated that oxygen is essential to both combustion and respiration [1]. Two major observations contributed to their discovery. The blood coming from the lung

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200 AD	Discovery of the respiratory system
1543	Concept of positive pressure ventilation
1670	Concept of negative pressure ventilation
1774	Discovery of oxygen
1865	Principle of homeostasis
1913	Discovery of the laryngoscope
1928	Negative pressure ventilation (iron lung) and poliomyelitis
1944	Intermittent positive pressure oxygen therapy and chest trauma
1952	Positive pressure ventilation and poliomyelitis
1963	Engström universal respirator
1967	Acute Respiratory Distress Syndrome
1970	Extracorporeal membrane oxygenation
1975	Optimum positive end-expiratory pressure
1987	Concept of baby lung
2000	Low tidal volume strategy
2015	Importance of driving pressure
2019	COVID-19 pandemic and strategic stockpile

Fig. 2.1 Timeline of the history of mechanical ventilation

is redder than the blood going into the lung indicating that "something" (that is oxygen) is brought into the blood when it passes through the lung. The fact that the temperature of the blood coming out of an organ is warmer led to the discovery of metabolism and carbon dioxide and water production as well as the concept of regulation of the internal environment or homeostasis by Claude Bernard in 1865.

2.3 The Dawn of Mechanical Ventilation

The first type of mechanical ventilators provided negative pressure ventilation using the Sauerbruch's method based on the differential pressure [3]. The concept of applying an external negative pressure ventilation was developed by John Mayow in 1670 and the first model was designed by John Dalziel in 1832. The first prototypes were built in 1876 and the first human use of a tank respirator or "iron lung" occurred in 1928 at the Boston Children's Hospital in the USA in a young child with poliomyelitis and respiratory failure (Fig. 2.2a). Iron lungs were widely used during the epidemics of poliomyelitis which disappeared with vaccination. A portable iron lung coined the "turtle shell" was well appreciated by the patients allowing them to be mobilized (Fig. 2.2b). Some patients remained on long-term mechanical ventilation: one patient remained on negative pressure ventilation for 16 years at the Mayo Clinic. I remember back in France taking care of patients with tracheostomy and on conventional positive pressure ventilator in the 1980s who had become part of the hospital.

When a gas exchange abnormality was also present, negative pressure ventilation appeared insufficient [4, 5]. The benefit of intermittent positive pressure oxygen therapy (IPPOT), precursor of intermittent positive pressure ventilation (IPPV)

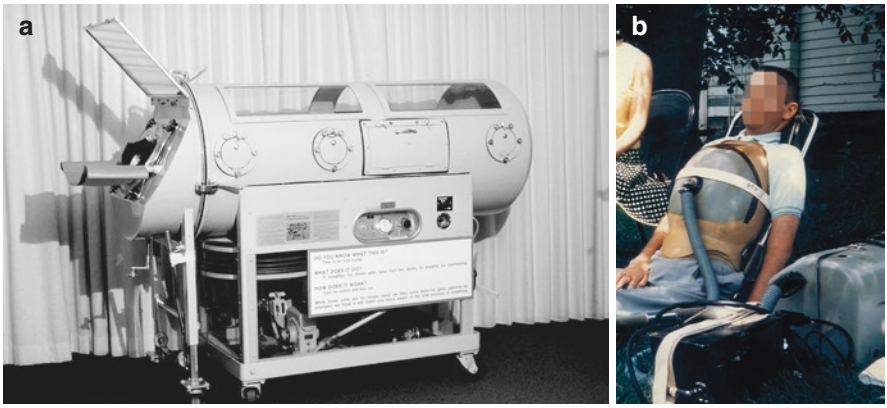


Fig. 2.2 (**a**) A negative pressure ventilator (iron lung) in display at the Mayo Clinic. (**b**) A portable iron lung (turtle shell) used by a Mayo Clinic patient

was discovered during the second world war to treat chest trauma that is the wet lung of trauma syndrome, also called posttraumatic respiratory insufficiency or respiratory distress syndrome [3], later coined acute respiratory distress syndrome (ARDS) by Ashbaugh in 1967 [4]. This led to the second type of mechanical ventilators which provided positive pressure ventilation. Their first use occurred during the 1952 poliomyelitis epidemic in Denmark, at the Blegdam Hospital in Copenhagen, in patients who underwent tracheostomy and positive pressure ventilation for "respiratory shock" [6]. The rapid decline in mortality associated with positive pressure ventilation led also to the rapid abandonment of the iron lungs. A flow sensitive breathing valve was developed by Bennett for high-altitude aviator oxygen delivery and applied to mechanical ventilation. In 1963, the Engström universal respirator was developed: a volume set, time-cycled with end-inspiratory pause [7]. First generation of positive pressure ventilators required electrical power. Aside explosion hazards, they were famous for their difficulty to adjust the acid-base status based on the actual tidal volume, sometimes unmasking a compensatory metabolic alkalosis in a setting of chronic respiratory acidosis. I remember vividly the challenge to prevent or correct alkalosis that could sometimes be severe. The development of blood gas analysis allowed prevention, detection and if necessary, correction of the acid-base status. The second generation of positive pressure ventilators were pneumatic device. The role of PEEP in preventing and correcting atelectasis was recognized [8] and sighs were often used as well as end-inspiratory pause. I remember that the Bennett MA-1 [9] had a PEEP limited around 17 cmH_2O and on the Siemens Servo Ventilator 900 series, the PEEP was easy to adjust on the lateral side of the machine but could be clogged by exhaled residues of nebulization. Other progresses included tracheal intubation, initially blindly by palpation of the neck and considered challenging. This led to the wider use of the laryngoscope discovered in 1913 independently by Chevalier Jackson and Henry Harrington Janeway and eventually the decrease of tracheostomy. In 1971, the introduction of an electronic feedback system with the SERVO provided a reliable way to set up a

ventilator. The latest generations of positive pressure mechanical ventilators are now equipped with microprocessor controls, various modes of ventilation and flow volume loop and other graphic displays. With time, emphasis has been made on ventilator synchrony like triggering, flow delivery, and adjustment to the respiratory drive, and include full ventilatory support like volume-controlled and pressure-controlled mandatory ventilation, airway pressure release ventilation, and partial ventilatory support like pressure support ventilation, proportional assist ventilation, neurally adjusted ventilatory assist and other proprietary modes of ventilation. Another technique, called high frequency oscillation, was short lived for its lack of efficacy. In the 1970s, Dr. Kolobow designed a successful membrane lung (known as the Kolobow lung) which was instrumental in the development of extracorporeal membrane oxygenation (ECMO) used when conventional mechanical ventilation has become insufficient to correct refractory cases of hypoxemic and hypercapnic respiratory acidosis [10].

Aside invasive modes of mechanical ventilation, noninvasive ventilation has also become popular with time. It was initially used in the 1940s for chronic conditions such as obesity-hypoventilation syndrome, obstructive sleep apnea, and neuromuscular diseases. Intermittent positive pressure breathing (IPPB), a pressure-cycled mode of noninvasive ventilation (IPPV), was popularized with the Bird Machine in 1955 and used in restrictive and chronic obstructive lung disease. It was short lived because of its brief duration of use but represents the precursor of pressure support ventilation [11]. Noninvasive ventilation has regained attention since the 1990s for acute conditions like chronic obstructive lung disease exacerbation, congestive heart failure exacerbation, and acute hypoxemic respiratory failure. It has become more attractive with the recognition of the potential deleterious effects of invasive mechanical ventilation. The interface was traditionally a mask or nasal pillows, but the use of a helmet has now gained popularity for its potential benefit in reducing intubation rates and mortality in patients with ARDS (Fig. 2.3).

2.4 Lessons Learned

The benefit of mechanical ventilation on reducing the work of breathing, providing adequate ventilation and oxygenation, is offset by the risk of ventilator-induced lung injury [2] that includes barotrauma with pneumomediastinum, pneumothorax and subcutaneous emphysema, biotrauma described as “the release of mediators by injurious ventilatory strategies, which can lead to lung and distal organ injury” [12] and more broadly speaking ventilator-associated complications. The deleterious effect of mechanical ventilation was already reported in 1944 by Macklin and Macklin who described the “malignant interstitial emphysema of the lungs and mediastinum as an important occult complication in many respiratory diseases and other conditions” [13]. The role of the PEEP, “helpful in combatting atelectasis and hypoxemia,” became prominent with the description of ARDS by Ashbaugh [4]. In 1975, Suter et al. proposed the “optimum end-expiratory airway pressure” or “best PEEP” “resulting in maximum oxygen transport (cardiac output times arterial oxygen content) and the lowest dead-space fraction [and] the greatest total static

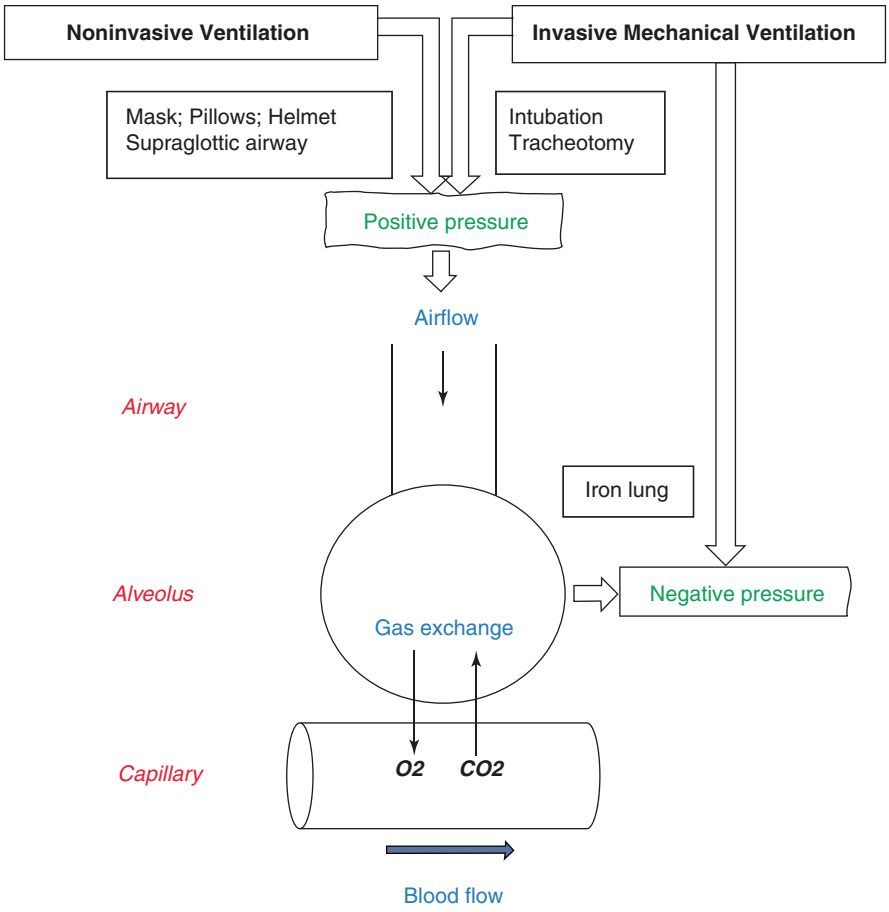


Fig. 2.3 The respiratory system coupled to the circulatory system and the different types of mechanical ventilation

compliance" [14]. There was also the need to prevent atelectasis associated with a low tidal volume and to minimize oxygen toxicity by limiting FIO_2. Ensued a time when patients were intubated and ventilated with high tidal volume (10 mL/kg of actual body weight), high PEEP, and often high peak and plateau pressure. I remember those times of frequent emergent chest tube placement and giant subcutaneous emphysema that came back in force with the current COVID-19 pandemic.

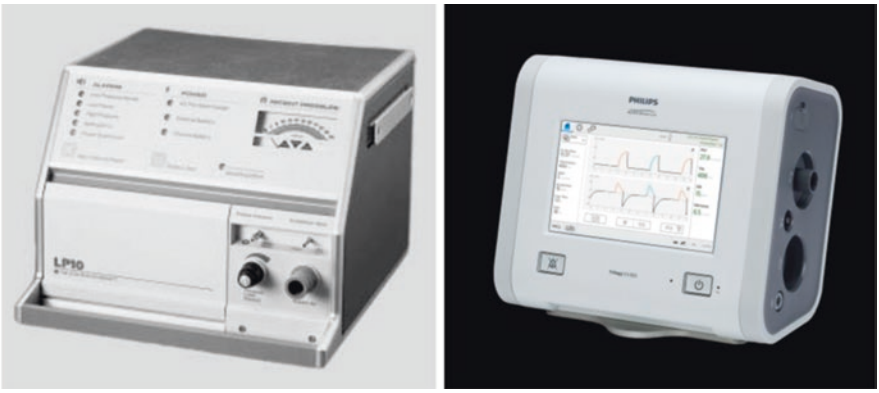
In the meantime, the concept of "baby lung" in ARDS was introduced by Gattinoni in 1987 from observation of the "non-homogeneous lung" in ARDS. Subsequently the concept of "shrinking baby lung" defined the progressive reduction in size and capacity for gas exchange in proportion to the severity of lung injury and emphasized the importance of avoiding the ventilator-associated lung injury vortex in acute respiratory failure by "following trends of gas exchange efficiency […], avoid labor breathing […], minimize oxygen demand and minute ventilation […], and prioritize low-stress tidal cycling" [15].

The benefits of minimizing tidal volume and plateau pressure were demonstrated by the landmark paper from the Acute Respiratory Distress Syndrome Network in 2000 that showed that an initial tidal volume of 6 mL/kg of predicted body weight and a plateau pressure of 30 cmH_2O of water or less resulted in decreased mortality when compared to a tidal volume of 12 mL/kg of and a plateau pressure of 50 cmH_2O or less [16]. While keeping a lower tidal volume and lower plateau pressure, the use of higher or lower PEEP resulted in similar outcome [17]. Further refinement in ventilator setting came with the concept of driving pressure, defined as tidal volume "intrinsically normalized to functional lung size" and measured as plateau pressure minus PEEP [18]. In 2015 in a landmark paper, Amato et al. showed that driving pressure change in relation to ventilator setting change was most associated with survival in ARDS and this should be considered when setting the ventilator [18]. These findings were confirmed by LUNG SAFE, a large observational study that showed that patients with a driving pressure of more than 14 cmH_2O on day 1 following intubation had a worse outcome [19].

The COVID-19 pandemic has demonstrated that the principles of lung protective strategy still apply. Intubation may be reduced using continuous positive airway pressure (CPAP). Neuromuscular blocking agents and prone positioning have been applied more frequently as well as rescue with extracorporeal membrane oxygenation. Yet, the proper titration of sedation remains a challenge. Finally, the timing of intubation (and extubation) should be judiciously decided to optimize the risk-benefit ratio of the invasive mechanical ventilation, while managing a de facto finite supply of ventilators or using a reserve inventory such as the US National Strategic National Stockpile Ventilators [20] (Fig. 2.4).

Examples of Ventilators Held by the Strategic National Stockpile in the United States

Covidien (Puritan Bennett) LP10 **Philips EV300**



https://www.aarc.org/resources/clinical-resources/strategic-national-stockpile-ventilator-training-program/

Fig. 2.4 Example of ventilators from the US National Stockpile during COVID-19 pandemic

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Airway Management in the Critically Ill

3

Sheila Nainan Myatra

3.1 Introduction

Tracheal intubation (TI) is one of the most commonly performed procedures in critically ill patients [1]. Critically ill patients have a *physiologically difficult* airway. The presence of physiological derangements such as hypoxaemia, hypotension, metabolic acidosis, neurological impairment, and right ventricular failure that may be present, increases the risk of complications during TI [2, 3]. Unlike in the operating room (OR), the often emergent nature of airway management, the critical illness, increased risk of aspiration, complex intubating conditions, limited access to advanced airway equipment and the presence of operators with varying level skills pose additional challenges during airway management in the ICU [4]. These are detailed in Table 3.1.

Several national studies and audits have shown high complication rates during TI in the critically ill. These complications include hypoxaemia, hypotension, arrhythmias, cardiac arrest and death [5–12]. The fourth UK National Audit Project report showed that major airway-related complications lead to death or brain injury in 61% of the cases in ICU, compared to 14% during anaesthesia [5]. Failure to use capnography, poor planning, poor recognition of high-risk airways, lack of advanced airway skills and equipment were major contributing factors. In the INTUBE Study, a large international prospective study on airway management in almost 3000 critically ill patients, at least one major adverse peri-intubation event was observed in 45.2% critically ill patients undergoing TI, with cardiovascular instability being the most prominent event, observed in 42.6% of patients. Severe hypoxaemia and cardiac arrest were observed in 9.3% and 3.1%, respectively. Patients experiencing major adverse events were at higher risk of ICU and at 28 days mortality after

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Table 3.1 Challenges associated with tracheal intubation in the critically ill

The ICU environment	
Infrastructure Equipment Monitoring Personnel Timing	Poor access to patient's head end, lack of space around the patient Advanced airway equipment such as a flexible bronchoscope, videolaryngoscope, etc. may not be readily available Patient monitors are usually placed at the head end of the bed may not be visible Availability of trained personnel for emergent TI may be variable An emergent TI may be required at any time of the day or night
The patient	
Airway assessment Challenging anatomy Risk of aspiration Preoxygenation Physiologically difficult airway Patient cooperation Waking up the patient	May be difficult or impossible due to lack of time or poor patient cooperative Maxillofacial trauma, cervical spine injury, airway injuries, burns, etc. The patient may not be fasted or have gastroparesis associated with critical illness Insufficient time for preoxygenation, inefficient preoxygenation caused by ventilation perfusion mismatch. Lack of physiological reserves may lead to rapid oxygen desaturation allowing less safe apnoea time for TI Poor physiologic reserve due to critical illness. The presence of hypotension, hypoxaemia, etc. may increase the risk of complications during TI The patient may be uncooperative due to critical illness Unlike in the OR, postponing airway management is not possible, as the critical illness mandates a definitive airway
The airway operator	
Variability in airway training, experience and skills Human factors	The airway operator may have limited airway management training and skills. An inexperienced junior doctor may be performing TI alone. The patient, ICU or operator-related factors, alone or in combination may produce a stressful situation for the operator which may affect performance. Cognitive overload, fixation errors, tunnel vision and poor communication may lead to an increased chance of errors

TI tracheal intubation, *OR* operating room

adjustment for underlying disease severity [13]. TI in critically ill patients is therefore a high-risk procedure [3].

Recognizing the high risk of complications in this vulnerable group, various international societies have developed guidelines to manage TI in the critically ill, with a focus on strategies to enhance patient safety [14–16]. Recent reviews have highlighted important strategies to minimize complications in these patients [17–20]. This chapter will provide updated evidence optimizing first-pass success and maximizing patient safety during TI in critically ill patients. Tracheal extubation and tracheostomy will not be covered.

3.2 Indications for Tracheal Intubation in ICU

The most common indications include:

1. Facilitation of invasive mechanical ventilation (inadequate oxygenation/ventilation, avoidance of hypercarbia, controlled hyperventilation, need for neuromuscular paralysis, postoperative elective ventilation).

2. Protection of the respiratory tract from aspiration of gastric contents.
3. Haemodynamic instability—shock, cardiac arrest, etc.
4. Relief of upper airway obstruction.
5. Tracheobronchial toileting.

3.3 Planning and Preparation for Tracheal Intubation

3.3.1 Clinical History and General Examination

The often emergent nature of TI in the critically ill may leave little or no time for obtaining a good clinical history and examining the patients. However, every effort should be made to obtain relevant clinical history and examination findings prior to TI. In addition to clinical history related to the present illness and comorbidities, specific history related to airway management such as the time of last oral intake, contraindications to use succinylcholine or other drugs, drug allergies, presence of dentures, loose or missing teeth, history of sleep apnoea and a previous history of a difficult TI should be elicited from the patient or family. Examination of the cardiorespiratory system and other systems should be performed along with a review of relevant laboratory investigations and imaging reports.

3.3.2 Airway Assessment

A thorough airway assessment may not be feasible due to lack of time or the patient being uncooperative. In a systematic review and meta-analysis of over 30,000 patients in the OR, the upper lip bite test (the inability to bite the upper lip with the lower incisors), a short hyomental distance, retrognathia and the modified Mallampati were shown to have a positive likelihood ratio of 14, 6.4, 6 and 4.1 respectively to predict a difficult airway [21]. The 12-point MACOCHA (**M**allampati class, presence of obstructive sleep apnoea OS**A**, **C**ervical spine mobility, mouth **O**pening, presence of **C**oma or **H**ypoxia, and presence of an **A**nesthesiologist) score (Table 3.2) proposed for airway assessment in the critically ill patients takes anatomical, physiological and operator skills into consideration to predict a difficult airway [22]. It is simple to perform and may be more suitable for use in critically ill patients.

3.3.3 Airway Cart and Checklists

An airway cart with all of the necessary items to facilitate TI, rescue oxygenation and haemodynamic support should be available near the patient prior to TI [14, 16]. Checklists may be helpful to ensure that the essential items and preparations have been undertaken prior to TI and are recommended in guidelines [16]. However, a randomized trial investigating the use of a written checklist prior to

Table 3.2 MACOCHA Score [22]

Factors	Points
Factors related to patient	
Mallampati score III or IV	5
Obstructive sleep apnoea syndrome	2
Reduced mobility of cervical spine	1
Limited mouth opening	1
Factors related to pathology	
Coma	1
Severe hypoxaemia	1
Factors related to operator	
Non anesthesiologist	1
Total score	12

TI in ICU compared to usual care found no difference in lowest oxygen saturation and lowest systolic blood pressure soon after TI between the groups [23]. The checklist used in this study however did not include interventions aiming at optimizing physiology, such as non-invasive ventilation, fluid loading, early use of vasopressors, etc. which may explain why it did not influence the selected outcomes. In addition, the participating centres were experienced with the use of checklists for other ICU procedures; therefore the control group may have had a high penetrance of the checklist items [23]. Nevertheless, a pre-intubation checklist, including essential strategies for physiological optimization, may be effective in less experienced hands, as observed following the implementation of the Montpellier intubation bundle, aimed at reducing life-threatening complications associated with TI [24].

3.3.4 Team Preparation

Considering the complexities and high risk of TI in ICU, advance team preparation and planning is paramount. Having two airway operators for TI, with at least one being experienced has been shown to reduce complications [24]. There should be clear communication among the team members about the airway concerns, airway plan, the roles and responsibilities of each team member, the backup plan and the rescue plan before proceeding to performing TI.

3.4 The Tracheal Intubation Procedure

The physiological derangements present in critically ill patients increase the risk of complications during TI. Hence it is essential to optimize patient physiology and adopt strategies to improve first-pass TI success, to avoid complications. These strategies have been outlined in Table 3.3.

Table 3.3 Important considerations during tracheal intubation in the critically ill

Airway intervention	Important considerations
Airway assessment	Consider using the MACOCHA score [22]
Team preparation	Presence of two operators (at least one experienced in airway management) Clear communication among the team members about the airway concerns, airway plan, backup and rescue plan with roles and responsibilities of the team members defined in advance
Patient positioning	Upright or 'ramped' position. This improves preoxygenation by preventing reduction in the FRC and may reduce the risk of pulmonary aspiration of gastric contents
Preoxygenation and apnoeic oxygenation	HFNO use for preoxygenation reduces intubation-related complications as compared with bag valve mask in patients who are not severely hypoxemic NIV should be the method of choice for preoxygenation in severely hypoxic patients Apnoeic oxygenation and gentle mask ventilation may be used after optimal preoxygenation to prolong the time to desaturation between induction and laryngoscopy, especially in patients at high risk for desaturation
Rapid sequence intubation	Should be considered in all patients
Induction of anaesthesia	Prefer intravenous ketamine or etomidate unless contraindicated
Neuromuscular blockade	Use intravenous rocuronium or succinylcholine unless contraindicated
Haemodynamics	Use fluids or vasopressors in the peri-intubation period to maintain haemodynamics Early use of vasopressors may be considered
Device selection for tracheal intubation	Use of a stylet or bougie should be considered for the initial tracheal intubation A VL should be immediately available for use. A hyper-angulated VL along with a rigid stylet should be preferred over a traditional geometry VL if available, in an anticipated difficult airway
Confirmation of tracheal tube placement	A mandatory confirmation using waveform capnography
Rescue oxygenation	Limit attempts at tracheal intubation to two Use face mask ventilation or a SAD to restore oxygenation In a failed intubation, if rescue ventilation is successful using mask ventilation or a SAD, consider performing a surgical or percutaneous tracheostomy or intubation through the SAD by an airway expert using a flexible bronchoscope Perform an emergency cricothyroidotomy if one cannot intubate and cannot ventilate the patient. Alternately, a surgical tracheostomy may be considered if a surgeon experienced to perform it is immediately available
Action following a difficult airway management	Monitor the patient for complications Treat airway oedema and examine the airway if required Documentation and counselling of the family and patient if feasible Team debriefing

(continued)

Table 3.3 (continued)

Airway intervention	Important considerations
Human factor considerations	Use a shared mental model for communication Follow an algorithmic approach to tracheal intubation to reduce cognitive load and improve the recognition and management of failure Advance training in both technical and non-technical skills for airway management

FRC functional residual capacity, *HFNO* high flow nasal oxygen, *NIV* non-invasive ventilation, *VL* videolaryngoscope, *SAD* supraglottic airway device

3.4.1 Patient Positioning

Whether *sniffing* or the *semi upright (ramped)* position (keeping external auditory meatus levelled with the sternal notch) is superior to improve glottic visualization and make TI easier compared with a patient positioned completely flat is still controversial [25]. A multicentre trial showed ramped position was associated with increased difficulty in TI compared to sniffing position. However, the ramped positioning used may be suboptimal in this trial and therefore these results should be interpreted with caution [26]. A large retrospective study showed that a combination of ramped plus sniffing positions significantly reduced complication rates in critically ill patients [27]. A prospective observational study showed improved first-attempt TI success when ramping was compared to supine position in the emergency department [28]. Though randomized clinical trials are lacking, the upright position does improve preoxygenation, prevents reduction in the functional residual capacity and may reduce the risk of pulmonary aspiration, which is much helpful in this vulnerable group of patients. Recent guidelines have recommended a head-up position, especially in patients at a high risk of aspiration or desaturation [14, 15].

3.4.2 Preoxygenation and Apnoeic Oxygenation

Critically ill patients are at a high risk of desaturation during TI [2, 3]. Oxygen delivery can be achieved using a simple face mask, standard or high flow nasal oxygen (HFNO), non-invasive ventilation (NIV) mask, or a combination of these devices. Standard nasal oxygen or HFNO can be continued during attempts at TI (apnoeic oxygenation). In addition to oxygenation, HFNO generates positive end-expiratory pressure [29]. NIV improves oxygenation PEEP delivery and ventilation by augmenting minute ventilation with pressure-supported breaths and decreasing the right ventricular preload and the left ventricular afterload [30].

Various preoxygenation and apnoeic oxygenation strategies to increase the safe apnoea period (time interval before desaturation after inducing apnoea) have been compared. In the PROTRACH study, patients without pre-existing hypoxaemia ($PaO_2/FiO_2 \geq 200$ mmHg) were randomized to HFNO (from induction to TI) or to oxygen by face mask for preoxygenation. Though HFNO failed to increase the lowest oxygen saturation during TI, patients in the HFNO group experienced a lower

incidence of TI-related complications [31]. The application of nasal cannula at 15 L/min during attempts at TI compared to standard care did not increase the lowest oxygen saturation during TI attempts in a randomized open-label study in 150 adults in a medical ICU [32]. In the FLORALI 2 study, critically adult patients undergoing TI were randomized to NIV or HFNO (from induction to TI). There was no difference in the incidence of severe hypoxaemia. However, in the subgroup of patients with a $PaO_2/FiO_2 < 200$, a potential benefit for NIV was seen [33]. Jaber et al. in a proof of concept study showed that adding HFNO for apnoeic oxygenation to NIV for preoxygenation was more effective in reducing the severity of desaturation during TI, compared to NIV alone [34]. More studies are required to confirm these findings.

Based on the recent literature, NIV seems to be the preferred method of choice for preoxygenation, especially in severely hypoxic patients. HFNO use has shown lesser complications related to TI as compared to bag valve mask preoxygenation in patients who are not severely hypoxaemic.

3.4.3 Induction of Anaesthesia

Drugs used for induction of anaesthesia can increase the risk of both haemodynamic and respiratory complications. Critically ill patients usually have reduced requirements for anaesthesia [35]. Ketamine and etomidate should be preferred in critically ill patients due to their positive haemodynamic profile [36]. Reducing the patient's minute ventilation during induction may blunt the respiratory compensation for metabolic acidosis, worsening acidosis and shock. Loss of a respiratory compensation during TI may exacerbate hypoxaemia present during induction [37].

3.4.3.1 Propofol

Propofol blunts the airway reflexes providing superior conditions for TI, even without the use of muscle relaxants. However, it may not be suitable in critically ill patients who are in shock, hypovolemic, with cardiac comorbidities having limited physiologic reserve, as there can be a precipitous fall in blood pressure and even bradycardia following its use. Retrospective studies have shown propofol use to be safe when various strategies to mitigate hypotension including fluid loading and vasopressor agents have been tried [38, 39]. Though ketamine and etomidate have been recommended as the induction agent of choice for TI in critically ill patients in various airway guidelines [14, 16], the INTUBE study showed that propofol still represents the most commonly used (42%) induction agent [13].

3.4.3.2 Etomidate

There have been concerns about adrenal suppression with the use of etomidate. A Cochrane analysis and a meta-analyses included observational studies and, showed that a single dose of etomidate was not associated with an increased mortality of critically ill patients [40, 41]. Corticosteroid supplementation may be considered if etomidate is used in patients with septic shock [42].

3.4.3.3 Ketamine

Ketamine is popular as an induction agent of choice unless contraindicated in critically ill patients, as it preserves the haemodynamics. No difference in intubating conditions or serious adverse events was found in a trial of 655 critically ill patients randomized to either etomidate or ketamine during RSI. However, there was a higher incidence of adrenal insufficiency in the etomidate group [36]. A study comparing the two agents in adult trauma patients showed no difference in first-pass success rates, ICU-free days, ventilator-free days or mortality used for RSI [43].

3.4.4 Controversies in Rapid Sequence Intubation

Critically ill patients may have gastroparesis associated with critical illness or may not be fasted at the time of TI. Thus, conventionally, a rapid sequence intubation (RSI) which involves administration of rapid onset agents (induction agent and muscle relaxant), cricoid pressure and avoidance of ventilation between induction and TI (to limit gastric insufflation and therefore pulmonary aspiration) is practised.

3.4.4.1 Use of Neuromuscular Blockade or Spontaneous Ventilation

RSI in critically ill patients is associated with greater first-attempt success and fewer TI-related complications [44–46] and should be considered in all patients. The use of neuromuscular blocking agents has been shown to improve mask ventilation, abolish upper airway muscle tone including laryngospasm, improve intubating conditions and optimize chest wall compliance. However, inducing apnoea in critically ill patients may result in rapid desaturation (secondary to loss of functional residual capacity, high metabolic rate, physiological shunt and ventilation perfusion mismatch), highlighting the importance of peri-intubation oxygenation and rescue oxygenation. The fear of inability to mask ventilate after giving neuromuscular blockade has led to reluctance in using these agents. However, recent guidelines recommend the use of these agents even during a cannot intubate, cannot ventilate emergency [14, 16]. No difference between the two agents with respect to oxygen desaturation, or successful first-pass TI was seen in a study comparing succinylcholine to rocuronium in critically ill patients [47]. Sugammadex may be used as an option for rapid reversal of rocuronium in an emergency [48]. However, there is limited data regarding its safety in critically ill patients. Succinylcholine may precipitate life-threatening hyperkalaemia in at-risk patients and thus should be used with caution.

Awake TI using a videolaryngoscope (VL) or flexible bronchoscope has a high success and safety in the OR. However, this requires patient co-operation and clinician expertise and may not be feasible in critically ill patients who are often unstable and uncooperative for this procedure.

3.4.4.2 Use of Cricoid Pressure

The use of cricoid pressure remains controversial. The Cochrane review concluded that more evidence is required [49]. A recent double-blind, randomized study

showed non-inferiority of sham versus cricoid pressure in preventing aspiration in patients at a high risk for aspiration [50]. Clinicians often have difficulty in identifying the cricoid ring. In addition, these is evidence that cricoid pressure may worsen the laryngeal view preventing successful TI and even mask ventilation [51, 52]. Nevertheless, several society guidelines still recommend the use of cricoid pressure during RSI [14, 16].

3.4.4.3 Mask Ventilation During RSI

Critically ill patients are at a high risk for hypoxaemia due to avoidance of ventilation between administration of neuromuscular blockade and TI during RSI. In the PREVENT study, 401 critically ill patients were randomized to receive mask ventilation or no ventilation between induction and TI [53]. Patients receiving ventilation experienced a lower incidence of severe hypoxaemia (oxygen saturation < 80%) without increasing the rate of pulmonary aspiration. Though this study was not powered for pulmonary aspiration, it provides some reassurance for gentle mask ventilation to limit hypoxia during RSI, especially in high-risk patients.

3.4.5 Haemodynamic Support During Tracheal Intubation

In the INTUBE study, there was a 42.6% incidence of cardiovascular instability following TI in critically ill patients [13]. The use of induction agents for anaesthesia, loss of sympathetic drive, hypovolemia and positive pressure ventilation may contribute to this. Haemodynamic instability is an independent predictor of adverse outcomes including mortality [12, 13]. The combination of hypotension and desaturation makes cardiac arrest even more likely [12]. Fluid loading and vasopressors are commonly used to prevent and treat hypotension. Fluid loading prior to TI as part of an TI bundle has shown to reduce life-threatening complications [24]. However, a recent trial showed no benefit with a routine fluid bolus prior to TI, although patients were not stratified by risk [54]. The early use of vasopressors instead to fluid loading to prevent hypotension during TI needs to be investigated.

3.4.6 Device Selection for Tracheal Intubation

3.4.6.1 Use of a Videolaryngoscope

A meta-analysis comparing direct laryngoscopy (DL) with VL for emergency TI outside the operating room, showed higher first-pass TI success rates with VL and fewer oesophageal intubations in the subgroup of ICU patients, though no difference in success rates was seen overall. The use of VL was associated with more life-threatening complications including hypotension [55]. A recent meta-analysis comparing VL with DL included nine randomized controlled trials with over 2000 critically ill patients. The use of VL did not improve first-pass success rate, even when evaluating the studies according to experience of the operator [56]. Some

studies included in these meta-analyses have shown higher incidence of severe life-threatening complications with VL use. An explanation given for these findings is failure to abort TI attempts when there is a clear laryngeal view using VL, leading to prolonged apnoea time and complications. There was heterogeneity in the studies included and some were of low quality. Nevertheless, though recent evidence does not support the routine use of VL for TI in ICU, VL improves glottic visualization as compared to DL making it an important tool for difficult airway management in ICU [57]. A hyper-angulated VL along with a stylet should be preferred over a traditional geometry VL if available, in an anticipated difficult airway. Future trials will better define the role of VL in ICU. Such trials should use first-pass TI success without complications as a primary outcome, rather than first-pass TI success rate alone [57].

3.4.6.2 Use of a Bougie

A recent randomized trial compared the use of a bougie with a tracheal tube and a stylet for TI in the emergency department in patients with at least one difficult airway characteristic [58]. There was significantly higher first-attempt TI success in the bougie group. This was a single centre study with operators experienced with the use of a bougie. Hence the generalizability of these findings is uncertain. Nevertheless, it seems reasonable to suggest that a bougie may be used to facilitate the initial TI in those experienced with its use.

3.4.6.3 Use of a Stylet

A stylet is commonly used to rescue a difficult tracheal intubation. The effect of routine use of stylet on first-pass success in critically ill patients has never been studied. Jaber et al. in randomized multicentre trial in 999 patients in 32 ICUs in France, compared the effect of TI using a tracheal tube with or without a stylet when performing direct laryngoscopy on first-attempt intubation success in critically ill adults. First-attempt intubation success was significantly better in the tracheal tube with stylet group compared to the tracheal tube alone group. There was no difference in the incidence of complications between the two groups [59].

The results of these two trials provide a strong rationale for the routine use of bougies and stylets for TI in the critically ill [60].

3.4.7 Confirmation of Tracheal Tube Position

Waveform capnography should be used to confirm TI (5–6 consistent waveforms with no decline) [14, 16]. Failure to use capnography resulted in 17 deaths or brain damage in ICU in the NAP4 report [5]. Oesophageal intubations and accidental tube displacements accounted for 82% of events leading to death or brain damage. This report strongly recommends the use of capnography for confirmation of TI in all critically ill patients [5]. However, despite the NAP4 report showing a high

incidence of adverse events due to failure to use capnography during TI, the INTUBE study published 10 years after this report showed that capnography was utilized in only 25% of patients to confirm proper tracheal tube placement. In addition, the study showed that capnography was not used in 70% of the patients who had an oesophageal intubation [13]. This highlights the importance of increasing global awareness and availability of capnography for improving the safety of airway management.

3.5 Rescue Oxygenation

If oxygen desaturation occurs during attempts at TI, mask ventilation should be performed to optimize oxygenation. Optimize mask ventilation with a two handed technique, using an oropharyngeal airway. If mask ventilation is inadequate, insert a supraglottic airway (SGA) device [14–16]. These devices form a seal around the laryngeal inlet and are inserted blindly. A second-generation SGA device should be preferred as it facilitates gastric decompression and provides a better laryngeal seal [14, 16].

Rescue ventilation using a SGA is often lifesaving in the critically ill. This skill should be learnt by all clinicians managing the airway of critically ill patients [61]. Since it is not used for routine airway management in ICU, critical care specialists are usually unfamiliar or untrained to use these devices. The NAP4 report concluded that in patients who were rescued using an emergent surgical airway, a SGA was not inserted in half of the cases. Moreover, it was often successful when inserted after performing a surgical cricothyrotomy, indicating that a cricothyroidotomy could have been avoided [5].

Following SGA insertion, successful rescue ventilation and restoration of oxygen saturation, one of the following options should be considered: TI through the SGA under bronchoscopic guidance by an airway expert or a surgical or percutaneous tracheostomy should be performed, since critically ill patients need a definitive airway for prolonged ventilation [14].

If SGA insertion is unsuccessful and the best attempt at mask ventilation, using an optimal technique and neuromuscular blockade is also unsuccessful an emergency cricothyroidotomy should be immediately performed, even if the oxygen saturation is preserved [14–16].

The optimal method for performing a cricothyroidotomy is still debatable. A surgical or wide bore cannula cricothyroidotomy (commercially available kits) should be performed. Needle cricothyroidotomy requires the use of trans-tracheal jet ventilation, which is usually not available in ICU.

Following an unanticipated difficult TI, monitoring the patient for further complications in essential. Watch for and treat airway oedema. Further examination of the airway by a specialist may be required, especially when airway trauma has occurred. Documentation of the airway difficulty along with counselling of the patient if feasible, or the family is essential [14].