Mechanical Ventilation and the CRNA: What You Need To Know

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CRNAs ARE EXPERTS IN managing and maintaining ventilation and pulmonary homeostasis. In a patient under the influence of anesthetic drugs, or who is critically ill, or for whatever reason has impoverished respirations, once the airway is secure, we frequently employ mechanical ventilation (MV) in caring for the patient.

The introduction of MV into the surgical operating room many years ago was absolutely transformative, especially when neuromuscular blocking drugs came into widespread use. The use of MV was not only instrumental in the birth of the intensive care unit (ICU) but served as an absolutely life-saving therapy in that environment. As deadly as the COVID-19 pandemic has been, administering care to those severely affected is greatly impaired without its use.

During ordinary clinical circumstances and before COVID-19, all patients in need of MV received it, unless they or their legal representatives declined it. However, concerns in the COVID-19 era changed. There were concerns that patients who otherwise would likely survive if they received MV might die because a ventilator was unavailable. In this type of public health emergency, the ethical obligation to prioritize individual patients' well-being may be overridden by public health policies that emphasize doing the greatest good for the greatest number. Such circumstances raise a critical question: when demand for ventilators and other intensive treatments outstrips the supply, what criteria should guide these rationing decisions?

While the ethical and public health issues associated with allocating scarce treatments, in this case, ventilators, are beyond the scope of this APEX Update, it does shed light, with laser-like focus, on the indisputable importance and versatility of an intervention that we may take for granted. But before we get granular about MV, let's go back in time for a crash course in its history on how we got to where we are today, some of which might prove surprising to you.

Five centuries of evolution to get us where we are today

The Greek physician Galen, who lived in the second century A.D., was the essential figure who introduced the importance of anatomy to the understanding of disease. His anatomical studies were confined to animals, and he falsely equated animal structure and function as being identical to that of humans. His studies of respiration led him to conclude that the physical act of breathing caused the heart to beat.[1] His influence and views remained essentially unchallenged for 1500 years; it was not until the Renaissance that many of his theories were refuted.

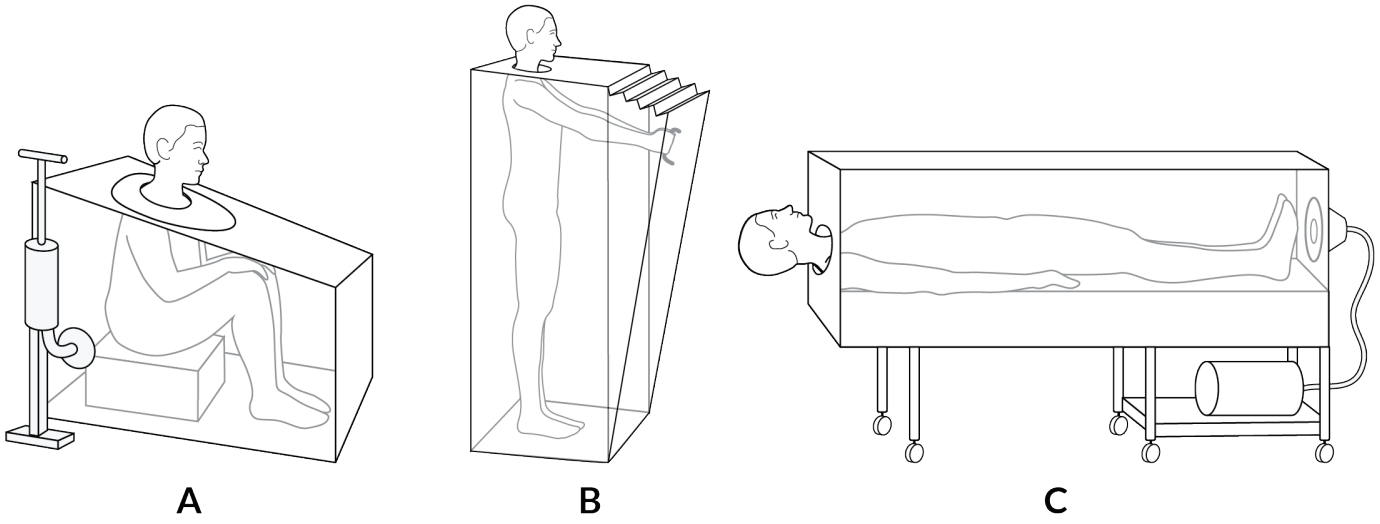
In the mid-16th century, Andreas Vesalius, a Professor of Anatomy working in Italy, relied on human cadaver dissection—much to the horror of church officials—in developing theories quite different from Galen's. A sentinel moment occurred in 1543 when he wrote what appears to be the first formal description of MV. "But that life may be restored to the animal, an opening must be attempted in the trunk of the trachea, into which a tube of reed or cane should be put; you will then blow into this, so that the lung may rise again and take air."[2] This was virtually forgotten and not incorporated into widespread medical practice for several centuries.

Fast-forwarding to the 17th and 18th centuries, several approaches were used to resuscitate patients, given that breathing was recognized as essential to life. Keep in mind that it was still unclear to the doctors and scientists why people breathed and why people became pulseless if breathing stopped. A prevailing theory was that people were unconscious and breathing slowed (or stopped) because of a lack of stimulation. This line of thought led to several unusual treatments whose goal was to stimulate a victim. These included rolling them over barrels, throwing them onto a trotting horse, flagellation, hanging them upside down, cooling them on ice, or using the fumigator, in which smoke was blown up the patient's rectum.

The discovery of oxygen in 1774, and recognizing its importance in respiration shortly thereafter, were milestone events. While there was some progress in ventilating distressed (or dying) people with mouth-to-mouth efforts, these were largely abandoned. It was believed that exhaled air lacked oxygen given the belief that another person's lungs had totally consumed it.

In the 19th century, ventilators emerged based on using sub-atmospheric pressure delivered around the patient's body to replace or supplement the work being done by their respiratory muscles. During the American Civil War, Jones invented a body-enclosing device where the patient sat in an airtight box with only the head protruding. An attached plunger was employed to decrease pressure in the box, creating subatmospheric pressure, causing inspiration, then used again to increase pressure in the box, causing exhalation. Jones' patent on the device noted that it "cured paralysis, neuralgia, seminal weakness, asthma, bronchitis, dyspepsia…" and many other disorders.[4] Hmmm, maybe a bit of hyperbole on behalf of Jones?

In the late 1870s, the first "practical" devices encapsulated just the thorax and were produced in France and called "spirophones." In Paris, public health and safety officials suggested that these be placed in strategic spots along the Seine River to aid drowning victims. The first "iron lung" to be widely incorporated was developed in the U.S. in 1929 to treat the first epidemic of polio victims.[5]



"A" Jones' negative pressure ventilator required the continuous attendance of someone to push and pull the piston, inspiring one design "B" where the patient created the pressure change, and eventually "C" a dedicated electric pump generated the pressure change giving rise to the "iron lung".

With eerie similarity to what we see with the COVID-19 pandemic, polio's resurgence marked a turning point in the evolution of MV and in the development of what was to become the ICU. Before this, MV was considered useful in isolated circumstances but was not widely used. An outbreak of the disease that overwhelmed Copenhagen in the early 1950s was, ironically, triggered by an international group of polio experts who attended a polio conference in the same city, likely bringing the virus with them.

The Copenhagen epidemic overwhelmed their resources, with up to 50 patients a day admitted to their specialty infectious disease hospital, many with the bulbar form that affected their respiratory muscles. Indicating just how little medical insight and care had evolved, many believed most of those who died had succumbed to renal failure due to bloodborne viremia, when in fact, it was due to frank respiratory failure. A local doctor, Bjørn Ibsen, who had trained in Boston, and aggressively challenged this, recommending that tracheostomy and positive pressure ventilation be employed.[6] Patient's under his care suffered far less mortality, and his approach was rapidly and widely adopted. A significant issue was that there were no positive pressure ventilators, necessitating the use of manual ventilation instituted by literally every pair of hands (in shifts) that could be summoned to duty. It also became rapidly apparent

out of necessity and logistics that it was best to manage these patients in a hospital's dedicated domain. This proved to be the birth of the ICU where specialized equipment, constant attendance of highly trained personnel, and intensive monitoring were all available in one location to render care.

From this point on, the developments in MV moved with astonishing speed. During surgical anesthesia, their potential use conspired with various economic incentives to catalyze the manufacturing of medical quality ventilators. Additional offspring included the development of training programs (e.g., respiratory therapists, critical care nurses, etc.), medical residency and fellowship tracks, and an explosion of specialty equipment design and manufacturing enterprises for the ICU (e.g., modifiable beds, infusion pumps, electronic monitors, etc.). It might be argued that the recognition for the value of MV gave rise to multiple attendant industries.

Mechanical ventilation comes of age, and there is no glass ceiling in sight

For starters, we can appreciate that we can deliver MV in any number of ways. As we saw from our brief historical overview, it can be delivered by altering the ambient pressure around the patient, and some modalities provide minimally invasive interventions such as the following:

- Nasal continuous positive airway pressure (NCPAP)
- Nasal intermittent positive pressure ventilation (NIPPV)
- Facemask ventilation
- Bi-level nasal continuous positive airway pressure (BiPAP)
- Continuous positive airway pressure (CPAP)
- High flow nasal cannula (HFNC)
- Helmet ventilation

All have their unique advantages, disadvantages, and applications. For our purposes in this APEX Update, we will focus on invasive MV, which we define as the positive pressure delivery of a selective gas mixture to the lungs via an endotracheal or tracheostomy tube.

There are many indications for invasive MV. Some are a function of drugs that have been administered (e.g., anesthesia, drug overdose, etc.). Others are due to pathophysiological processes (e.g., pulmonary edema, pneumonitis, Guillain-Barré syndrome, etc.). Below is an incomplete list of conditions where MV may be employed:

- Infectious or aspiration pneumonitis
- Noncardiogenic or cardiogenic pulmonary edema
- Intravascular volume overload
- Airway tumor
- Tracheal stenosis
- Upper airway angioedema
- Severe exacerbation of chronic obstructive pulmonary disease
- Severe asthma
- Pulmonary thromboembolism, amniotic fluid embolism
- Myasthenia gravis, amyotrophic lateral sclerosis, Guillain-Barré
- Muscular dystrophy and other myotonic syndromes
- Pneumothorax and trauma (flail chest, multiple rib fractures)
- Respiratory inadequacy due to general anesthesia and drug effect

Again, let's emphasize that this is only a partial list. As CRNAs, our experience is generally due to some form of drug-induced respiratory inadequacy. But we often care for patients coming from the ICU to the OR (and vice versa) who are receiving MV. Additionally, we are often called upon to care for patients with underlying conditions that merit our careful consideration in planning their ventilatory management.

We institute MV to fully or partially replace spontaneous breathing, perform the dual tasks of ventilating the lungs, and to facilitate gas exchange in those unable to manage independently. A mantra held dear by many experienced CRNAs is "if you are wondering if you should intubate, you probably should!" Likewise, if you vacillate about whether or not MV should be instituted, it seems the prudent path is to do so. The bottom line is that if there is an indication for MV, initiate it early in the course of management and don't delay the decision until the need becomes emergent.

With MV, a predetermined composition of the gas is propelled into the patient's central airways, then moves into the alveoli. With lung inflation, intra-alveolar pressure increases. Once a termination threshold is reached (volume or pressure or even time defined), the ventilator ceases the forward flow of gas with central airway pressure now falling. Passive expiration of gas flows from the higher pressure in the alveoli to the lower pressure in the central airways and exits the patient.

Understanding and selecting the mode of ventilation

Like any drug administration decision, once we decide to institute MV, it should be accomplished in a patient-centered manner. Matching the ventilation mode with the patient's unique needs must also factor in practical considerations, including the clinician's familiarity and experience with the options and what the institution's equipment has to offer. While various ventilatory strategies exist, when we refer to the mode of ventilation, we are primarily referring to the method of inspiratory support.

In discussing the different modes and ventilatory strategies, not all equipment is equivalent. Furthermore, most of our in-the-OR anesthesia workstation ventilators aren't outfitted with all the "bells and whistles" of the more ample ICU ventilators.

The volume-limited mode of MV

This is also referred to as "volume-controlled" or "volume-cycled" ventilation. Depending on the equipment available, we can customize the peak flow rate, flow pattern, volume to be delivered, respiratory rate, positive end-expiratory pressure (PEEP), and the percentage of oxygen (FiO_2). Inspiration ceases once the inspiratory time set has elapsed, something we can adjust by altering the inspiratory to expiratory time (I:E ratio) either by a dedicated dial or by increasing the peak inspiratory flow rate, which will decrease inspiratory time, increase expiratory time, and decrease the I:E ratio.

Airway pressure depends on the ventilator settings and patient-related variables such as compliance and airway resistance. A high airway pressure may be a function of an excessively large tidal volume, a high peak flow, poor compliance, or increased airway resistance.

Within the umbrella of volume-limited ventilation are the following:

- Controlled MV (CMV) where the delivered minute ventilation is a function of the tidal volume and delivered breath rate that is set.
- Assist control (AC) is where we set a minimal minute ventilation by selecting a basic tidal volume and rate. If the patient triggers an additional breath, the ventilator will deliver the preset tidal volume.
- Intermittent mandatory ventilation (IMV) is akin to assist control. Here we set a minimal minute ventilation in the usual fashion. The patient can increase it as they desire—but any extra breath that the patient initiates will only be as large as what the patient can generate independently.
- Synchronized intermittent mandatory ventilation (SIMV) is where the ventilator attempts to deliver the mandatory breaths in synchrony with the patient's inspiratory efforts. The ventilator allows the patient a chance to breathe. If the patient makes an inspiratory effort during a window of time determined by the IMV rate, the ventilator delivers a breath in response to the patient's inspiratory effort. However, if no inspiratory effort is detected by the ventilator, a time-triggered breath is delivered.

The pressure-limited mode of MV

This is also termed pressure-cycled ventilation and involves the CRNA setting the inspiratory pressure level, I:E ratio, respiratory rate, PEEP, and FiO_2. Inspiration ends after delivery of the preset inspiratory pressure being achieved.

In this mode of MV, the tidal volume can vary considerably as it is the product of a complicated interaction among the preset inspiratory pressure level, the patient's compliance, their airway resistance, and the ventilator circuit tubing

resistance. Clinically, the tidal volumes will be larger when the preset inspiratory pressure level is high, there is good patient compliance or negligible airway resistance, and/or there is little resistance from the ventilator circuit tubing.

While tidal volume may vary, the peak airway pressure remains constant during pressure-limited ventilation. This avoids dangerously higher pressures that may be inadvertently delivered to the patient's lungs due to changing conditions. However, individual tidal volumes can vary with consequential effects on the delivered minute ventilation.

The very same modes that are used in volume-limited ventilation can be employed in pressure-limited ventilation:

- During pressure-limited controlled mechanical ventilation, which many of us call pressure control ventilation (PCV), the minute ventilation is determined by the set respiratory rate and inspiratory pressure level. The patient does not initiate a larger minute ventilation above that set on the ventilator.
- During pressure-limited assist control (AC), the set respiratory rate and inspiratory pressure level determine the minimum minute ventilation. The patient can increase the minute ventilation by triggering additional ventilator-assisted, pressure-limited breaths.
- During pressure-limited intermittent mandatory ventilation (IMV) or synchronized intermittent mandatory ventilation (SIMV), the set respiratory rate and inspiratory pressure level determine the minimum minute ventilation. The patient can increase the minute ventilation by initiating spontaneous breaths.
- Pressure regulated volume control (PRVC) is also termed pressure-controlled volume guaranteed (PCVG). In this mode, the ventilator computer adjusts applied pressure up or down based on whether the exhaled tidal volume is above target (applied pressure for next breath is decreased) or below target (applied pressure for next breath is increased). This attempts to hold the tidal volume constant. Once the ventilator computer decides on the pressure to be applied, the breath delivered is a true pressure controlled, time cycled breath. This is a sophisticated mode that is available on select ventilators.

What does the evidence reveal?

We know that MV is an essential component of anesthetic and critical care management. In the case of a patient with acute respiratory failure, it is a necessity. Both volume-targeted and pressure-targeted ventilation modes are used in the ICU setting, with the latter mode being increasingly used in the OR. A recent meta-analysis in the prominent journal *Chest* examined their effectiveness in a head-to-head review.[7]

Thirty-four studies met the inclusion criteria for the study and were the basis of the analysis. Comparisons between the modes of ventilatory support did not show any difference for compliance or gas exchange, and there was no difference between modes in terms of hemodynamics, work of breathing, or clinical outcomes.

Despite the two modes having different working principles, this study's summary statement was that the clinical evidence does not suggest any difference in the outcomes. The study included all the reasonable and identified trials involving patients with acute respiratory failure, enhancing generalizability, and attempted to include only quality physiologic studies. As is often the case in biomedical studies like this one, some of the included trials were small and varied in quality despite meeting inclusion criteria.

Another study, a Cochrane review, examined three randomized controlled trials involving a total of 1089 participants recruited from 43 ICUs worldwide, including the U.S.[8] Risk of bias of the included studies was considered very low. To achieve the most valid findings, only data regarding mortality and barotrauma was reported as they were the most consistent and reliably reported outcome data.

The authors lamented that there is still insufficient evidence to confirm or refute whether pressure-controlled or volume-controlled ventilation offers any advantage for people with acute respiratory failure due to acute lung injury or acute respiratory distress syndrome (ARDS). Again, they recommended that "larger trials, better controls, and longer and closer patient follow up" are needed to solidify thought in the area.

Confusion, complexity, and sheer "volume" of terms

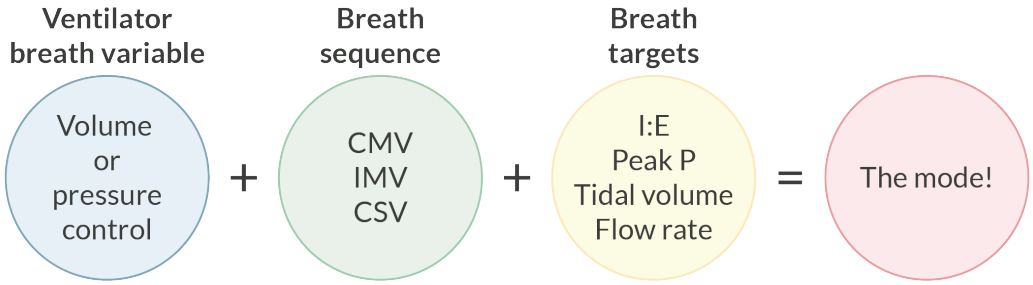
The number of modes of ventilation has grown enormously over the last four decades. In this APEX Update, we found one popular textbook focused on respiratory equipment that included 174 unique names of ventilator modes on 34 different ventilators.[9] The level of complexity in terms of the actual number of unique modes exceeds even this as most ICU ventilators allow the clinician to customize the ventilatory mode by activating various features. The result is that there are many more unique modes (in terms of different patterns of patient-ventilator interaction) than there are names indicated on the ventilators, in operators' manuals, or in textbooks.

There are other ventilation modes that perhaps are better termed "ventilation strategies". These include high-frequency ventilation (HFV), inverse ratio ventilation (IRV), adaptive support ventilation (ASV), and neurally adjusted ventilatory assist (NAVA), just to mention a few. But these fall into a different category than this fundamental APEX Update is focused on and will not be discussed.

Given the magnitude of ventilatory modes and strategies, is this a recipe for confusion or what?!?

One way to simplify this is to create a kind of conceptual "mind map" about ventilators and how they can be configured to produce different modes. Consider this diagram as an aide to help you envision how a different selection in each section can result in the desired mode. Note too that even in this simple illustration, the number of permutations can be quite high!

A conceptual map: What exactly is a ventilation 'mode'?



We know we can injure the lungs with our ventilation strategy, so be careful!

MV can most certainly induce lung injury.[10] There are several ways that this can happen during MV. These include

1. injury to the force-bearing entities of the lung, the elastin and collagen fibers. Elastin provides the rebound effect once it has been stretched during inspiration and promotes passive exhalation like a rubber band pulled at both ends then released. Collagen is folded together like an accordion in the resting (exhaled) phase and continues to unfold during inhalation until a maximum large breath is taken, limiting overexpansion. Exceeding their volume and/or pressure limits can cause either barotrauma or volutrauma.
2. atelectrauma, which refers to damage to both the epithelial lining and to the surfactant-producing system. This is due to repetitive shearing factors of back and forth opening and closing in a disjointed manner. It is primarily a function of the impact of stress and strain maldistribution in a lung with a mixture of unevenly ventilated pulmonary units.
3. oxytrauma, especially with the use of a high FiO_2. This refers to a host of ills, including direct tissue toxicity, absorption atelectasis, and free-radical formation that can lead to inflammation and cell death.
4. diaphragmatic muscle atrophy. Though not a direct "lung injury" issue, MV can cause a phenomenon called ventilator-induced diaphragmatic dysfunction (VIDD). MV can lead to rapid onset disuse atrophy involving the diaphragmatic muscle fibers which can develop within the first day of MV.[11]

5. dys-synchrony between the patient and the ventilator. It can induce diaphragmatic and pulmonary injury and cause delays in weaning the patient from MV, creating a vicious cycle of ventilator dependency.

The practical application of safe ventilation in everyday practice: what have we learned?

The selection of a ventilation mode is often a matter of provider preference and experience, with variation occurring in the context of select patient conditions. With this pragmatism in mind, there are some general principles that are well-grounded in clinical research and experience that serve as fundamental guiding principles.

- While it was once common practice to use large intraoperative tidal volumes (VT), there is a very robust body of evidence describing its risk of inducing harm, urging against this approach. Rather, lower VT is now well accepted, safe, and effective in the range of 6–8 mL/kg based on their lean body weight, especially in the obese patient.
- Intraoperative PEEP remains controversial as there is conflicting evidence (benefit vs. harm). While modest amounts of PEEP may be beneficial, higher values are associated with an increased risk of hypotension frequently requiring vasoactive drug intervention.
- Likewise, FiO_2 is controversial, with some still suggesting that high levels have a preventive effect on surgical site infections. Although that is, at best, unsettled, there are significant concerns that gas absorption atelectasis may occur, setting the stage for postoperative pulmonary complications.
- And, while some advocate periodic lung recruitment maneuvers such as a lung expansion maneuver consisting of three manual bag ventilations with a maximum pressure of 40 cm H_2O, this too remains controversial despite seeming quite plausible. The optimal timing, frequency, number of successive bag ventilations, and target holding pressure remains unclear. Until that all gets a bit firmer, proceed cautiously with the use of recruitment maneuvers.

The best course of action, especially regarding PEEP, FiO_2, and recruitment maneuvers, is to carefully and cautiously titrate them to the desired effect using the least effective 'dose' of each.

The application of "adjuncts" to enhance MV

There may be clinical circumstances when the best effort to improve gas exchange or to protect the lungs from our interventions is just not working well, and the severity of the condition (disease, trauma, unique patient issues) demands considerations of what we will term "adjuncts" to MV.

Adjuncts to MV include the following and will not be discussed in detail, but merit our consideration and discussion when traditional MV approaches are falling short of the clinical goal. These approaches are often considered "last-ditch" adjuncts, and one or more are finding application in those suffering severe respiratory inadequacy in the COVID-19 pandemic.

1. Enhanced exchange of respiratory gases:
   - Extracorporeal membrane oxygenation (ECMO)
   - Pump-less interventional lung assist (iLA)
   - Dead space reduction techniques.
2. Reduction in metabolic demand:
   - Pharmacological paralysis, sedation
   - Permissive hypercapnia
   - Therapeutic hypothermia
3. Techniques to improve ventilation and lung perfusion:
   - Prone positioning
   - Nitric oxide
   - Prostaglandin analog administration

Progress has been made in clinical trials with respect to the above adjuncts. However, the reality is that definitive information is still lacking for its use in the most challenging and nuanced patient circumstances. The COVID-19 experience accelerates that clinical experience, and future reports may shed more light on what adjuncts work best in a given patient.

Clinical contemplations

- What is your "routine" approach to MV in the operating room? Are you primarily using volume- or pressure-limited approaches? Do you approach ventilator mode choice on a case-by-case basis?
- Do your anesthesia workstation ventilators allow you to provide more "ICU-like" modes to your patients? In what way?
- Given the COVID-19 experience, have you been involved in ventilator management outside of your traditional operating room setting? What were your concerns, if any, for the safety of the patient?
- If you are transferring a patient from the ICU to the OR for surgical anesthesia, what unique ventilation modes are being used? How are you managing the patient if those modes aren't available to you in the OR during your care?

Summary and conclusions: personalized mechanical ventilation is where it's at!

We've come a long way in seven decades since the Copenhagen polio outbreak and the interventions of Bjørn Ibsen, representing the birth of MV as we know it. Along the way, many strategies have evolved, providing us with a range of modes from which to select. Each carries the risk of MV-induced injury if not carefully considered and applied in the context of the unique patient.

Advances in the prevention of injury from MV might best be achieved by exquisitely tailoring the MV approach to the physiological and pathophysiological characteristics of the individual patient. This requires a good understanding of the different ventilatory modes and how they can best be tailored to the individual patient.

There is still much to be learned and applied. For example, in an ideal world, to truly tailor MV to a particular patient, it may require developing and adopting clinical respiratory monitoring techniques. Monitoring of pleural pressure with esophageal manometry enables clinicians to account for derangements in chest wall mechanics when titrating ventilator pressures, allowing bedside quantification of the mechanical stresses applied to the lung.[12] Estimation of pleural pressure might also provide a useful guide to set PEEP to prevent lung de-recruitment.

Because patient inspiratory effort can't be predicted directly from applied ventilator pressures or even by physical examination, direct measures of inspiratory effort are required to properly titrate partially assisted ventilatory support. Bench research in animal models demonstrates that these can be achieved with various technologies, including esophageal manometry, electromyography, and even ultrasound. How this plays out in practical clinical applications remains to be seen.

The bottom line: selecting a ventilatory mode and strategy for a given patient should be very personalized. And what about the advances that have been achieved over these most recent seven decades? Well, there's a good chance that we've got a lot of learning and a lot of progress ahead of us in the years to come.

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