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The Ventilator Book has been the go-to reference for physicians, advanced practice providers, respiratory therapists, fellows, residents, and students working in the Intensive Care Unit since 2012. Dr. William Owens explains, in clear language, the basics of respiratory failure and mechanical ventilation. This is a guide to keep in your jacket pocket, call room, or in the ICU.

The third edition combines the content of the original book with key chapters from *The Advanced Ventilator Book* into one comprehensive reference. Chapters have been updated to reflect new developments in critical care medicine and the experience gained during the COVID-19 pandemic. The book is divided into sections on physiology and technology; conventional modes and basic concepts; and unconventional modes and advanced concepts. As always, there are chapters for initial ventilator setup, adjustments, and troubleshooting. Patient-ventilator dyssynchrony, rescue therapies for ARDS, and ECMO are also covered.

The goal of *The Ventilator Book* is to demystify mechanical ventilation for the nonexpert practitioner and to emphasize safe, patient-based critical care. This edition lives up to the intent of the best-selling original, which is to make difficult concepts easy to understand.

First Draught Press

Owens

The Ventilator Book

First Draught

THE VENTILATOR BOOK

Third Edition

William Owens, MD

First Draught Press

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First Draught Press
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Medicine is an ever-changing discipline, and the subject matter of this book is no exception. While the author has done his best to ensure that this book reflects contemporary evidence-based practice, new developments in the field may supersede the material published here. Only properly trained and licensed practitioners should provide medical care to patients with respiratory failure. Nothing in this book should be construed as advice regarding the care of a specific patient or group.

Third Edition

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To Lorien—my wife, best friend and fellow adventurer, who has stood by me through thick and thin for nearly 20 years. You are the one who encouraged me to write the first edition in Pittsburgh, and you have given me the necessary prodding to write the second and third editions as well. I couldn't have done this without you.

William, Zach, and Amelia—you three are the best kids I could ever hope to have. Not many families have conversations like ours, and I'm pleased that all three of you know what a ventilator is and the indications for ECMO. I'm proud to be the dad of three happy, independent, naturally curious people who are all determined to make their marks on the world.

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Introduction

So, here you are in the Intensive Care Unit at 3:30 in the morning. The Emergency Department has just admitted a patient to your service—a young man with a rather sudden onset of fever, rigors, and respiratory distress. He had to be intubated in the ED and the ventilator seems to be alarming with a nerve-racking frequency. His chest X-ray looks horrible, with diffuse infiltrates and consolidations. The ICU respiratory therapist looks at you and asks the question you have been dreading since the patient arrived— "Doctor, what vent settings do you want?"

This is a familiar story for those of us who spend a lot of time in the ICU, and since the advent of the COVID-19 pandemic, it's an experience that just about every student and resident has at least once during his or her training. Mechanical ventilation can be intimidating—it has its own terminology, not all of which makes sense; it's a life-sustaining technology, and misapplication can have serious consequences; and practitioners of mechanical ventilation tend to talk in esoteric ways about what the ventilator is doing. This can confuse even the smartest practitioner.

To make things worse, there aren't a lot of practical resources for busy clinicians who just need some quick guidance on how to adjust the ventilator. Don't get me wrong—there are *plenty* of great textbooks on mechanical ventilation. And, if you have the time, they are well worth reading. The operative word, however, is "time." Reading a hundred pages on the pros and cons of pressure-controlled ventilation may be a good use of an afternoon in the library but it's wholly impractical while taking care of patients in a busy ICU. What's necessary is a how-to guide, and that's why I first wrote this book in 2012. It may seem basic to experienced ICU clinicians, but then again, it's written for the nonexperts in the room. I would also venture to say that most success in critical care medicine comes from doing the basic stuff right on a consistent basis.

This is now the third edition of *The Ventilator Book,* which I have enjoyed putting together. I have combined some new material with updated chapters from the second edition of *The Advanced Ventilator Book* to create a

more comprehensive single resource. I would like to thank many of my readers for their feedback on previous editions, and I hope you'll find that it had an impact on this one.

Since there's only one author, this book will be biased. Not too much, I hope, but I'm not delusional enough to think that my approach is completely objective. Like everyone else in medicine, personal anecdote and experience has shaped my practice.

This book is intended to teach you about the practical aspects of mechanical ventilation. The chapters are short, and each can be read easily within 15-20 minutes. Here, you'll learn to speak the language and understand the rationale for why things work and why intensivists do what they do. I also believe that understanding the "whys" of what we do is important, and I've included some chapters on respiratory physiology and technology.

At this point, it's necessary for me to point out that while this book is chock-full of great advice, none of it is specific to the care of any individual patient. Have any of your faculty ever told you that the patients don't read the textbook? They're right. Every patient needs an individualized approach. Believe it or not, my lawyer didn't make me write this. *It's just common sense*.

Philosophy of Mechanical Ventilation

The art of medicine consists of amusing the patient while Nature takes its course.

—Voltaire

Mechanical ventilation is a wonderful tool. The birth of modern-day critical care occurred in Copenhagen in 1952, when Bjorn Ibsen realized that positive pressure ventilation could save lives during a polio epidemic when the iron lungs (a negative pressure ventilator) were failing. The most common reason for admission to a medical intensive care unit is the need for mechanical ventilatory support. The combination of endotracheal intubation and positive pressure ventilation has likely saved hundreds of thousands, if not millions, of lives.

Likewise, artificial ventilation has prolonged the lives of thousands of people afflicted with spinal cord injuries and devastating neuromuscular diseases. Ventilators attached to wheelchairs permit patients with these conditions to engage in life, to pursue their interests, and to generally live lives that would not have been possible a half-century ago. Truly, this invention has had a positive effect on many, many people.

As is the case with any technology, however, there is the potential for misuse. It is essential that anyone working in an intensive care unit remember the Third Commandment—that the ventilator is a means of support, and not a cure for any condition. In other words, it is folly to believe that the application of mechanical ventilation can reverse chronic lung disease, malignancy, congestive heart failure, or any of the myriad diseases and injuries that result in respiratory failure. The ventilator exists to maintain the respiratory and metabolic functions of the lungs until the patient recovers from his or her illness. It cannot make the patient better by itself. This is actually a point lost on many physicians, who believe that small tweaks and adjustments to the ventilator will accelerate the patient’s recovery from acute respiratory failure.

If it is important for physicians to understand the natural history and

trajectory of a patient's disease, it is equally important that the physician present this information to the patient and his family in concise, understandable, and even blunt terms. A life spent connected to a ventilator may be acceptable to a patient with amyotrophic lateralizing sclerosis, who may require mechanical ventilation but can otherwise speak, interact, and engage in what he considers an acceptable quality of life. It is a different matter entirely for a patient suffering from a massive intracerebral hemorrhage who is comatose, and is expected to remain comatose for, if not the rest of his life, a great deal of it. While the patient or his family may consider this to be a worthwhile existence, it behooves the physician to inform them of the stark realities of preserved life on a ventilator (including the medical, social, and financial ramifications) before they pursue this treatment option.

So, what is a dedicated, caring physician, nurse, or respiratory therapist to do? Unsubstantiated optimism can be harmful, but so can overly pessimistic nihilism. Most patients with respiratory failure who recover from the inciting illness or injury will recover; true ventilator dependence, meaning a need for mechanical ventilation more than a year afterward, is rare. Here's what we can do:

1. Protect the lung from iatrogenic injury. Use an evidence- and physiology-based approach to ventilator settings.
2. Promptly and aggressively treat the inciting illness or injury.
3. No disease is effectively treated with starvation. Proper nutritional support is very important.
4. People aren't meant to lie in bed all day. Unless the patient is comatose, in shock, or has profound respiratory failure, it's time to start getting him out of bed and into a chair. Walking, even. I'll add that this, of course, requires a strong dose of common sense. Mobilizing a patient with an open sternum might not be a good idea. But it's surprising how many patients lie flat on their backs for their entire ICU stay. Not healthy.
5. When the patient seems to be recovering, start assessing his readiness for extubation every day.
6. Be patient. It might take longer than you think.
7. Once it's evident that the patient will require prolonged mechanical ventilation, get on with the tracheostomy. There's no need to wait an

arbitrary number of days.

8. Pay attention to the little things like DVT prophylaxis, skin care, and preventing delirium.
9. Be patient. And….
10. Remember that your patient is a fellow human being with wants, needs, cares, and concerns that may be strikingly similar to your own. He deserves to be spoken to, even if he can't speak back. He deserves respect, even though he may not be able to return that respect. He deserves the basics of human kindness and touch. Remember that he has placed his life in your hands. *Your job is not an easy one, and not one that most people can do.* The recognition that you have positively affected the life of another person in a way that few can is the greatest reward of this great profession.

Chapter 1
Initial Settings

**Note on measurements—unless otherwise specified, all airway pressures are measured in cm H_2O. Gas pressures (PaO_2, $PaCO_2$) are measures in mm Hg. All tidal volumes are expressed as mL/kg of predicted body weight (PBW).*

Modes of Ventilation

There are several different modes of ventilation, and each ventilator manufacturer has its own (usually trademarked) name for them (PRVC, VC+, CMV with Autoflow, ASV, PAV, Volume Support, and the list goes on and on). This can be intimidating at first—who's to know what to pick? Fortunately, like medications, all of these have a generic name as well. That's all you really need to know, because all of the modes on the different ventilators available for sale will be essentially the same (just with a different trade name).

Each mode of ventilation has its strengths and weaknesses. No mode is perfect, and no mode is useless. It's best to pick the mode that best suits the patient's needs at the time. Each of these modes is discussed in more detail in the following chapters, but here's a brief overview.

Assist-Control Ventilation

Assist-Control Ventilation is the mode of choice in most circumstances. It allows the ventilator to essentially take over the work of breathing and is preferred when a patient has acute cardiac or respiratory failure. It provides full respiratory support. If the patient wants to breathe over the set rate, he can; when he triggers the ventilator, he gets the full breath with minimal effort.

Upside: Takes over the work of breathing; clinician can choose to set a tidal volume (volume control) or an inspiratory pressure (pressure control).

Downside: A tachypneic patient will get the full tidal volume on every breath, so without adequate sedation this could lead to significant respiratory alkalosis or air trapping. This can be a problem in patients with COPD or asthma.

SIMV with Pressure Support

SIMV also can provide full ventilator support and is a very popular mode. Like Assist Control, the clinician can choose a tidal volume or an inspiratory pressure. The major difference between SIMV and Assist Control is what happens when the patient initiates a breath— in A/C, he gets the full tidal volume; in SIMV, he gets whatever he can pull (usually with the help of pressure support).

Upside: Can take over the work of breathing but allows the patient more spontaneous breathing than in assist-control. Can be useful for weaning support gradually.

Downside: If the machine rate is not set high enough, an unstable patient can get fatigued due to excessive work of breathing. If the pressure support is not set high enough, spontaneous breaths may be fast and shallow, which also leads to fatigue.

Pressure Support Ventilation

PSV doesn't have a set rate—instead, it allows the patient to breathe on his own and "boosts" each breath with a pressure that the clinician selects. It's used in conjunction with CPAP to improve alveolar recruitment. PSV is used in patients who are either intubated for reasons other than cardiac or respiratory failure (altered mental status, jeopardized airway) or for weaning. It can also be used when the patient has a severe metabolic acidosis—if he has a pH of, say, 6.88 and a HCO_3 of 4, his respiratory drive will be markedly elevated and a mode like assist-control may not be able to meet his metabolic demands.

Upside: Allows the patient to set his own rate and pattern of breathing, which

is more comfortable; spontaneous breathing has salutary effects on hemodynamics and VQ matching.

Downside: There's no backup rate, so if the patient goes apneic nothing will happen until the alarms sound. Unstable patients will fatigue rapidly if the work of breathing is imposed on them, even with high levels of pressure support.

Unconventional Modes

Airway pressure release ventilation (APRV) and high frequency oscillatory ventilation (HFOV) are used to treat severe hypoxemia. They are seldom the first-line option for acute respiratory failure and will be discussed later in the book. For now, just focus on the modes already listed (A/C, SIMV, PSV).

Ventilator Settings Based on Pathophysiology

Restrictive Lung Disease

Examples: ARDS, aspiration pneumonitis, pneumonia, pulmonary fibrosis, pulmonary edema, alveolar hemorrhage, chest trauma

Restrictive lung diseases are associated with a reduction in respiratory system compliance. The lungs want to collapse. In other words, it's hard to get air in and easy to get air out. The ventilation strategy is to recruit vulnerable alveoli, prevent cyclical alveolar closure, provide adequate oxygenation, and to minimize volutrauma from overdistension.

The initial mode should be one that takes over the work of breathing for the patient. Assist-control, using either volume-controlled or pressure-controlled ventilation, is the mode of choice.

For volume-controlled ventilation:

1. Tidal volume of 6 mL/kg PBW
2. Rate of 14-18 breaths per minute, with a decelerating flow pattern
3. FiO_2 100% at first; reduce to 60% if $SpO_2 \geq 88\%$
4. PEEP of 5-10 cm H_2O, depending on the degree of hypoxemia. Remember, the more opacification in the lungs on the chest X-ray, the

more PEEP will be needed to reduce intrapulmonary shunting.

5. If hypoxemia persists, increase the PEEP until the SpO_2 is 88% or better. Don't exceed 20.
6. After adjusting the PEEP, check the plateau pressure. If the P_{PLAT} is more than 30 cm H_2O, decrease the tidal volume until the P_{PLAT} is less than 30. Don't go below 4 mL/kg PBW.

For pressure-controlled ventilation:

1. PEEP of 5-10 cm H_2O, depending on the degree of hypoxemia
2. FiO_2 100%; reduce to 60% if $SpO_2 \geq 88\%$
3. Inspiratory pressure of 15-20 cm H_2O
4. Rate of 14-18 breaths per minute
5. Inspiratory time adjusted to keep the I:E ratio 1:1.5 or higher. The I-time is usually 1.0-1.5 seconds. A rate of 20 and an I-time of 1.0 seconds has an I:E ratio of 1:2 (one second inspiration, two seconds expiration). A rate of 15 with an I-time of 1.5 seconds has an I:E ratio of 1:1.7 (1.5 seconds inspiration, 2.5 seconds expiration). This is displayed on the ventilator screen.
6. If hypoxemia persists, increase the PEEP until the SpO_2 is 88% or better. Don't exceed 20 cm H_2O.
7. Look at the exhaled tidal volume. If it exceeds 6 mL/kg, lower the inspiratory pressure until the tidal volume is in the 4-6 mL/kg range.

After initiating ventilation, check an arterial blood gas. 15-20 minutes is enough time for gas exchange to equilibrate.

Make changes in the respiratory rate to change the $PaCO_2$ (a higher rate lowers the $PaCO_2$, and vice versa). Leave the tidal volume in the 4-6 mL/kg range, keeping the P_{PLAT} at 30 cm H_2O or less. Remember that lung protection is more important than normal ventilation—a pH of 7.15 or better is acceptable and it's not worth injuring the lungs with overdistension (in the form of high tidal volumes) to get a normal pH or $PaCO_2$.

Lower the FiO_2, keeping the PaO_2 between 55 and 70 mm Hg and the SpO_2 between 88% and 94%. There's nothing to gain from keeping the PaO_2 above

this range, with few exceptions. Patients with traumatic brain injury sometimes require a higher PaO_2, usually in conjunction with brain tissue oxygen monitoring. Victims of carbon monoxide poisoning also benefit from breathing 100% oxygen.

Obstructive Airways Disease

Examples: COPD, Asthma

Obstructive lung disease is associated with an increase in respiratory system compliance and an obstruction to expiratory airflow. It's easy to get air in, but hard to get it out.

The ventilation strategy is to rest the respiratory muscles, provide adequate oxygenation, and reduce hyperinflation.

Assist-control ventilation is usually the mode of choice, and volume-control is preferable to pressure-control. SIMV with PS can also be used, however, as long as the rate and PS are set high enough to prevent tachypnea and fatigue. High airway resistance and high peak inspiratory pressures characterize exacerbations of COPD and asthma, even though the P_{PLAT} may be significantly lower. Using pressure-control in this situation leads to very low tidal volumes. Volume-control guarantees that the desired tidal volume will be delivered.

1. Tidal volume of 8 mL/kg PBW. Lower tidal volumes can lead to air trapping and worsening hyperinflation.
2. Rate of 10-14 breaths per minute
3. Inspiratory time adjusted to keep an I:E ratio of 1:3 or higher. In obstructive airways disease, air gets in easily but has a hard time getting out due to narrow, inflamed bronchioles and bronchi. Give the air some time to escape.
4. With asthma, applied PEEP will worsen hyperinflation. With COPD, PEEP can be used to splint open airways that are prone to collapse. This is because COPD is characterized by dynamic airway obstruction, while the obstruction is fixed in an asthma exacerbation. A good starting point for both is a PEEP of 0, or ZEEP—zero applied end-expiratory pressure.

5. FiO_2 of 100% to start; lower this to 60% as long as the SpO_2 remains 88% or better.

Sometimes, patients with COPD or asthma will remain tachypneic despite adequate sedation. In assist-control, every patient-triggered breath delivers a full tidal volume, and this can lead to air trapping or severe respiratory alkalosis. If this is the case, switching the mode to SIMV may help.

Severe Metabolic Acidosis

Examples: Salicylate poisoning, septic shock, toxic exposures, acute renal failure, diabetic ketoacidosis

The normal response of the respiratory system in the setting of metabolic acidosis is to hyperventilate. CO_2 is a volatile acid, and the lungs can rapidly eliminate this acid from the body in an attempt to bring the pH closer to normal. In a patient with a HCO_3 of 4 mEq/L, for example, the $PaCO_2$ will be 14-15 mm Hg if there's appropriate respiratory compensation. This requires a very high minute ventilation to accomplish.

It is very difficult to set the ventilator to provide a high minute ventilation, even if you set the rate to be 30-35 and the tidal volume to be 800-1000 mL. Patients with severe metabolic acidosis will often breathe in when the vent is trying to breathe out, and vice versa—this leads to significant patient-ventilator dyssynchrony and alarming of the machine. More consequentially, the volume and pressure alarms that are normally helpful will actually work against the patient by limiting the minute ventilation that can occur.

Consider the aforementioned example—a patient who has a pH of 6.88 and a HCO_3 of 4 needs a $PaCO_2$ of 14-15. If he's intubated and sedated, and the vent settings are put in the "usual" range, his $PaCO_2$ may rise to 25-30. In the setting of severe acidemia, this increase in CO_2 will cause his pH to fall to 6.6 or so, which will most likely lead to a cardiac arrest.

The best way to deal with this situation is to let the patient's naturally high respiratory drive work in his favor.

1. Use the *bare minimum* of sedation to intubate and avoid neuromuscular

blockers entirely.

2. Set the vent mode to be Pressure Support Ventilation.
3. CPAP (a.k.a. PEEP) 5-10 cm H_2O, depending on the degree of hypoxemia
4. Pressure Support (PS) of 10-15 cm H_2O. Adjust if needed to allow the patient to breathe comfortably; most of the time, 10 cm is enough PS.
5. Allow the patient to have a high minute ventilation—it may be 18-25 L/min or higher. Don't be alarmed to see him pull spontaneous volumes of 1000-2000 mL. The high minute ventilation will keep the pH up while the cause of the metabolic acidosis is being treated.

Key Concepts for Other Clinical Situations

- The left ventricle likes PEEP—increasing the intrathoracic pressure lowers preload and afterload, which is beneficial in acute cardiac failure due to left ventricular dysfunction (either systolic or diastolic).
- The right ventricle, on the other hand, doesn't care for PEEP very much. Increased intrathoracic pressure can increase pulmonary vascular pressures and stress the thin-walled RV. In situations where RV failure is present (massive pulmonary embolism, worsening pulmonary hypertension), use more FiO_2 and less PEEP (ideally 10 cm or less) to maintain oxygenation.
- When there is acute brain injury, be it from stroke, hemorrhage, trauma, or something else, the priority with mechanical ventilation is the maintenance of adequate oxygenation. Aim for an SpO_2 of 94-98% and a PaO_2 of 80100 mm Hg. PEEP may increase the intracranial pressure, but it seems to be significant only when the PEEP is 15 or higher. Hypoxemia, on the other hand, definitely increases intracranial pressure. Therefore, use what it takes to maintain adequate cerebral oxygenation.
- Hyperventilation ($PaCO_2 < 32$) lowers intracranial pressure, but it works by causing cerebral vasoconstriction. In other words, it works by making the brain ischemic. This may be helpful if a patient is about to herniate, and you need 5 minutes to get the mannitol in or 10 minutes to get to the OR. Prolonged hyperventilation, on the other hand, worsens brain ischemia and has no lasting effect on intracranial hypertension. Aim for a normal (35-40) $PaCO_2$.

Chapter 2

Quick Adjustments and Troubleshooting

Problem: Gas Exchange Abnormalities

These are ways to adjust the ventilator based on the arterial blood gas. Obviously, the patient's condition should dictate what's done. The adjustments are in order of preference.

PaO_2 Too Low

Assist-Control, SIMV: increase PEEP, increase FiO_2

APRV: increase P_{HIGH}, increase T_{HIGH}, increase FiO_2

HFOV: increase mean airway pressure, increase FiO_2

$PaCO_2$ Too High

Volume Assist-Control or SIMV: increase rate, increase tidal volume

Pressure Assist-Control or SIMV: increase rate, increase driving pressure

APRV: increase the gradient between P_{HIGH} and P_{LOW}, decrease T_{HIGH}, increase T_{LOW}

HFOV: decrease the frequency, increase the amplitude, increase T_I%, allow a 5 cm cuff leak

$PaCO_2$ Too Low

Volume Assist-Control or SIMV: decrease rate, lower tidal volume

Pressure Assist-Control or SIMV: decrease rate, lower driving pressure

APRV: increase T_{HIGH}, lower P_{HIGH}, decrease T_{LOW}

HFOV: increase the frequency, lower the amplitude, decrease T_I%

These are problems that you'll be called about. As always, the first thing you should do is examine the patient. Remember your ABCs and use this guide to help you figure out what's wrong.

Problem: High Peak Airway (P_{AW}) Pressures

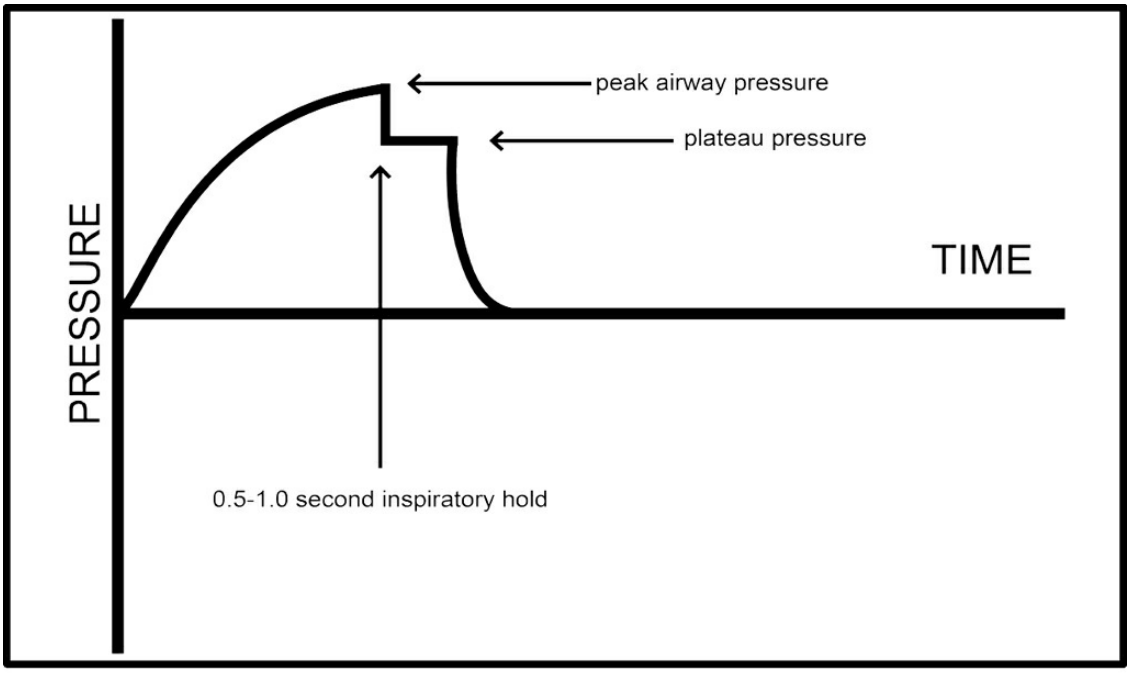
Your first step should be to perform an inspiratory pause and measure the plateau pressure (P_{PLAT}). The plateau pressure represents the alveolar pressure, while the peak pressure is a combination of the alveolar pressure and airway resistance.

High P_{AW}, Low P_{PLAT}—this means the problem is high airway resistance.

- Kinked endotracheal tube—unkink the tube
- Mucus plugging—pass a suction catheter
- Bronchospasm—inhaled bronchodilators
- Too narrow of an endotracheal tube—change the tube, or accept higher P_{AW}

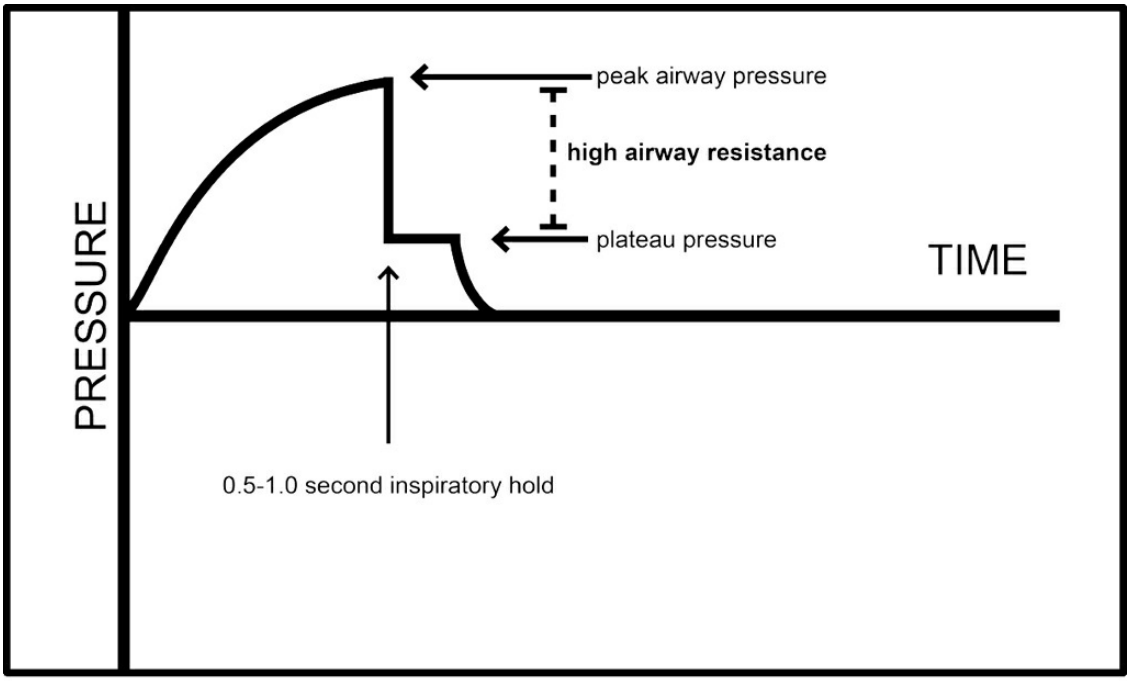
High P_{AW}, High P_{PLAT}—this means the problem is in the lungs.

- Mainstem intubation—pull the endotracheal tube back into the trachea
- Atelectasis of a lobe or lung—chest percussion, or bronchoscopy to open up the airway
- Pulmonary edema—diuretics or inotropes
- ARDS—use a lower tidal volume, higher PEEP strategy
- Pneumothorax—chest tube



The plateau pressure, or P_{PLAT}, represents the equilibration of pressures throughout the lungs when flow is stopped. This is the best assessment of the alveolar pressure.

The *difference* between the peak airway pressure and the plateau pressure represents the resistance of the conducting airways. This is normally < 5 cm H_2O.



An increase in the gradient between the peak and plateau pressures indicates high airway resistance.

Problem: Dynamic Hyperinflation (Auto-PEEP)

This is usually due to inadequate time for exhalation. High airway resistance (bronchospasm, COPD, mucus plugging) makes it worse. On exam, the patient's abdominal muscles will contract forcefully during exhalation. Neck veins may be distended, and you may hear loud wheezing. The ventilator's expiratory flow waveform will not return to the baseline of zero flow.

- Lower the ventilator rate, usually between 10-14 breaths per minute
- Shorten the inspiratory time to keep the I:E ratio in the 1:3 – 1:5 range
- Keep the tidal volume in the 6-8 mL/kg range—a higher tidal volume will often slow the patient's spontaneous respirations
- Increase the inspiratory flow to 60-80 liters per minute if the patient seems to be "air hungry"
- Adequate sedation with narcotics will help blunt a tachypneic response
- Treat bronchospasm with inhaled bronchodilators and systemic steroids

Problem: Sudden drop in SpO_2

New or worsening hypoxemia is always cause for alarm. The first step is to exclude mechanical problems or tube displacement.

- Disconnect the patient from the ventilator and bag him
- Make sure the tube is in place (use either color-change or waveform capnometry if there's any doubt about the tube) and that breath sounds are present and equal
- Obtain an arterial blood gas
- Chest X-ray—this will show you worsening infiltrates, pneumothorax, pulmonary edema, atelectasis, or new effusions
- Always consider pulmonary embolism as a cause for new hypoxemia in an ICU patient, and have a low threshold for diagnostic studies
- Absent breath sounds on one side—pull the endotracheal tube back a few centimeters
- Absent breath sounds on one side, even with the tube in the right place —think pneumothorax, or mucus plugging with complete atelectasis of the lung
- Tension pneumothorax should be suspected if breath sounds are absent on one side and if the patient is hypotensive. Distended neck veins and tracheal shift away from the affected side are supportive but not always seen. The treatment is immediate needle decompression and placement of a chest tube.

Problem: Fighting the Ventilator

Before sedating or paralyzing a patient for "fighting the ventilator," you should always check **TSS—T**ube, **S**ounds, **S**ats. Make sure that the endotracheal tube is in place and not obstructed, that breath sounds are present and equal, and that the patient is not hypoxemic. Other things you should look for are:

- Dynamic hyperinflation (see above for how to treat this)
- Untreated pain, especially in trauma and surgical patients
- Make sure the vent is providing an adequate rate and tidal volume
- Switch to assist-control ventilation, if the patient is getting fatigued

- Search for other causes of distress—cardiac ischemia, fever, abdominal distension, neurologic deterioration, etc.

Problem: Change in End-Tidal CO_2

First, look at the waveform. If there is no waveform, it means one of three things:

- The endotracheal or tracheostomy tube is not in the trachea
- The tube is completely occluded
- The $ETCO_2$ sensor is faulty

Obviously, the first two are serious emergencies and should be dealt with immediately. The third is diagnosed only after ruling out the first two.

If the waveform is present, then look at the $ETCO_2$ value. With a significant change in the $ETCO_2$, an arterial blood gas should be obtained as well to see what the $PaCO_2$ is.

Rising $ETCO_2$ and $PaCO_2$—this indicates either increased CO_2 production or alveolar hypoventilation.

- Fever
- Malignant hyperthermia
- Thyrotoxicosis
- Suppressed respiratory drive without a sufficient ventilator backup rate

Falling $ETCO_2$ with unchanged or rising $PaCO_2$—the widening gradient between the two suggests an increase in dead space ventilation.

- Pulmonary embolism
- Falling cardiac output (cardiogenic or hypovolemic shock)
- Dynamic hyperinflation with autoPEEP

Falling $ETCO_2$ and falling $PaCO_2$—indicates an increase in alveolar ventilation.

- Pain
- Agitation
- Fever
- Sepsis

Chapter 3

The Eleven Commandments of Mechanical Ventilation

I. Thou shalt mind thy patient's **COMPLIANCE** and measure it daily.

- Compliance is the change in volume divided by the change in pressure. **Dynamic** compliance is the exhaled tidal volume divided by the dynamic change in pressure (Peak minus PEEP). **Static** compliance is the exhaled tidal volume divided by the static pressure differential (Plateau minus PEEP). If there's a big difference between the two, increased airway resistance is usually to blame.
- Normal respiratory system compliance is about 100 mL/cm H_2O; normal for a ventilated patient is 70-80.
- Falling compliance can mean fluid overload, developing pneumonia or ARDS, pneumothorax, or many other bad things.
- Improving compliance usually means the patient is getting better, at least from a pulmonary mechanics point of view.

II. 'Tis nobler to **INTUBATE** and **VENTILATE** than to

needlessly allow a patient to suffer the slings and arrows of critical illness.

- Intubating a critically ill patient is never a sign of weakness; rather, it is a sign of decisiveness.
- A few of the indications for intubation are refractory hypoxemia, hypercapnia, a jeopardized airway, shock, and great metabolic disturbances.

III. Thy mechanical ventilator is merely a means of **SUPPORT** and offers no curative properties in itself.

- It's a mistake to think that the ventilator itself can help the patient. It merely allows the patient to survive until he recovers.
- A ventilator has only three therapeutic benefits:
  1) Guaranteed delivery of high levels of oxygen
  2) Positive pressure to reduce intrapulmonary shunt (from atelectasis, ARDS, pneumonia, pulmonary edema, etc.)
  3) Providing the work of breathing until the patient is able to do it himself

IV. Thou shalt be familiar with the **ABUNDANCE** of **MODES**, as no one is perfect for every situation and no one is completely useless.

- While you may have your preferred mode, remember that you can ventilate most any patient with any given mode as long as you set the ventilator properly.
- Some patients will seem to prefer one mode over another. I don't know why this happens, but it does.

Deal with it and don't be afraid to find out what vent settings suit the patient best.

V. Thou shalt mind the **TIDAL VOLUME** closely and without fail, lest the lungs suffer from excessive distension.

- Of all the studies done on mechanical ventilation in acute lung injury and ARDS, the ***only*** thing that seems to affect survival is the use of excessive tidal volumes.
- Your resting tidal volume is 4-8 mL/kg of your predicted body weight. Your patient's should be as well.
- The patient's actual body weight should not be used for this calculation. Carry a table, memorize the formula, or download an app to figure out the PBW. You will need the patient's height and gender (both usually easy to obtain).
- Be wary of physicians who confidently tell you that the plateau pressure is more important, or that 7, or 8, or 9 mL/kg is better than 6 in ARDS—while they may be right, they possess no evidence to support their claims.

VI. Thou shalt **OPEN** thy patient's lungs and **KEEP THEM OPEN.**

- Positive end-expiratory pressure is used to recruit collapsed alveoli and to prevent them from closing during exhalation.
- This helps to restore at least some functional residual capacity and reduce intrapulmonary shunt.

- A general rule is that if you can see white stuff in the lungs on the chest X-ray, increasing the PEEP is better than using high levels of oxygen for correcting hypoxemia.

VII. For the **PERFECT ABG** is a mythical creature and should not be pursued lest the patient suffer grave harm in the form of barotrauma and volutrauma.

- It's more important to protect the patient from harm than to blindly pursue a "normal" blood gas, especially if it means using excessively high tidal volumes or ventilator pressures.
- All decisions regarding ventilator settings should be made with the whole patient in mind. Permissive hypercapnia is perfectly acceptable in status asthmaticus but not in the patient with cerebral edema.
- In most cases, a PaO_2 of 55 is adequate.

VIII. Thou shalt not allow thy shocked patient to **FATIGUE**, but instead provide the ventilator support necessary for him to recover.

- In the setting of shock, hemorrhage, or severe sepsis, work of breathing can account for 40-50% of a patient's basal energy expenditure. Mechanical ventilation should be used to take over this work until the underlying cause has been treated adequately.
- Assist-control ventilation is one of the best ways to do this and is the preferred mode most of the time in these situations.

- There are many theories about exercising the diaphragm and allowing the patient to “work out” on SIMV or CPAP/PSV, but no one has proven that it helps (and it may in fact be harmful).
- Assist-control, with a daily spontaneous breathing trial if indicated, is a simple formula that is also very effective at minimizing the time a patient stays on the ventilator.

IX. Thou shalt seek out **DYNAMIC HYPERINFLATION** wherever it may be found, and treat it, for ‘tis an insidious beast!

- Hyperinflation is also known as auto-PEEP or breath stacking. It occurs when the patient can’t get all of the air out before the next breath starts.
- If unchecked, dynamic hyperinflation can lead to discomfort, hypercapnia, hypotension, and even PEA arrest. Suspect it in all patients on the vent who have obstructive lung disease and look for it even in patients who don’t. If the $PaCO_2$ keeps going up as the rate is increased, hyperinflation is the likely culprit.
- Treat this condition by slowing the ventilator rate, extending the time for exhalation, and treating bronchospasm. A small measure of applied PEEP may help prevent airway collapse during exhalation.

X. Verily, a **SPONTANEOUS BREATHING TRIAL** should be performed readily and daily on all patients whose conditions permit.

- No one is good enough to reliably predict which patients can be extubated on a given day.
- A spontaneous breathing trial (SBT) should be done whenever the reason for intubation (severe hypoxemia, coma, shock, bronchospasm) has resolved. The SBT can be in the form of a T-piece or low-level pressure support ventilation.
- Don’t be afraid to act on the results of the trial. If the patient looks ready, extubate him. The occasional reintubation is not a sign of failure. In fact, if you never reintubate a patient, you’re probably waiting too long to extubate the others.

XI. Thy Respiratory Therapist is the ordained **KEEPER OF THE VENT** and should be treated with utmost esteem.

- Do not make any changes to the ventilator settings without the RT present. If you want to experiment with different settings to see what happens, call the RT first.
- While you may know what you’re doing, you probably don’t know how to reset all the alarms, sensors, etc. that have to be adjusted when significant changes are made. It’s also the RT’s responsibility, and if you make changes without notifying him it makes a difficult job even harder.

Chapter 4

Acute Respiratory Failure

Acute respiratory failure is one of the most common reasons for admission to the intensive care unit. The majority of cases will require some sort of positive pressure ventilation, either from a mask (CPAP, BiPAP) or an endotracheal tube. Obviously, this is important. There's a reason why A and B come first in the ABCs of resuscitation—without adequate gas exchange (oxygenation being the most important), the patient can die within minutes. Many times, the physician has to treat acute respiratory failure before he can figure out the whys and hows of what happened. That's OK! Once the patient is stabilized, however, the detective work begins.

Acute respiratory failure, according to the textbook by Parrillo and Dellinger, is "the inability of the respiratory system to meet the oxygenation, ventilation, or metabolic requirements of the patient."[1]

Let's break this definition down:

- "The respiratory system": More than the lungs. Obviously, the lungs are the major players, but disorders of the upper airway, chest wall, cardiovascular system, and neurologic system can cause significant respiratory dysfunction.
- "Oxygenation requirements": Type I respiratory failure is defined as a PaO_2 less than 60 mm Hg. The first priority in treating patients with acute respiratory failure is to correct hypoxemia!
- "Ventilation requirements": Type II respiratory failure is a $PaCO_2$ greater than 50 mm Hg, *with* a pH less than 7.30. The pH is important in distinguishing acute from chronic respiratory failure.
- "Metabolic requirements": This is often forgotten, but the lungs have a

key role in maintaining metabolic homeostasis. CO_2 clearance by the respiratory system is adjusted to balance out metabolic derangements. Likewise, oxygen intake and delivery to the tissues begins in the lungs.

- "Of the patient": Probably the most important part of the definition. A particular patient may have "normal" blood gas numbers but still require respiratory support. Conversely, another patient may have *terrible* numbers but not require any kind of acute intervention. Like everything else in medicine, start with the history and physical exam.*

Common Diagnostic Testing

Arterial Blood Gas: to determine whether or not respiratory failure is present, assess the metabolic status of the patient, and to determine (in part) the cause of respiratory failure. Co-oximetry can help diagnose carbon monoxide poisoning and methemoglobinemia.

Chest X-ray: to diagnose cardiac failure, pneumonia, pneumothorax, pleural effusion, and a whole lot of other diseases. Also, helpful if it's normal—a clear X-ray and hypoxemia should make you consider a pulmonary embolism.

CT Chest: for a better look at the thoracic structures; if done with angiographic technique, it can diagnose pulmonary embolism and aortic dissection.

Bronchoscopy: to diagnose inhalational injury, foreign body, upper airway obstruction, pneumonia, and alveolar hemorrhage.

Hypoxemic Respiratory Failure

Hypoxemia poses the most immediate threat to the patient. Vital organs like the brain, heart, etc. depend on a continuous delivery of oxygen to use for energy production. That's why just about all resuscitation efforts begin with giving the patient supplemental oxygen (by nasal cannula, mask, or endotracheal tube). The pathophysiologic causes of hypoxemia are:

1. Shunt
2. Ventilation-Perfusion (VQ) Mismatch
3. Diffusion limitation
4. Dead Space
5. Low FiO_2 (fraction of inspired oxygen)
6. Low P_B (barometric pressure)
7. Alveolar hypoventilation

Of the things in this list, low FiO_2 and low P_B are the easiest to rule in or out. Low FiO_2 is seen in house fires (from consumption of oxygen by the flames) and anesthetic gas mishaps. Low P_B includes things like airplane cabin depressurization and being at extreme altitude. Look around--if you're not in an airplane, the building isn't on fire, and you're not on top of a mountain, these can be discarded from the differential diagnosis. Good! That leaves us with five things to worry about instead of seven. Diffusion limitation is really significant in only a few diseases like pulmonary alveolar proteinosis—most of the time the problem is VQ mismatch. Down to four.

Sorry to introduce math into a clinical discussion, but it's inevitable. If you want to do the job you must have the tools, and one important tool in this field is the *Alveolar Gas Equation***.** This equation predicts what the alveolar pressure of oxygen should be.

Alveolar Gas Equation

$$P_AO_2 = [(P_B - P_{H2O}) \times FiO_2] - (PaCO_2 / RQ)$$

where P_AO_2 is the partial pressure of oxygen in the alveolus, P_B is barometric pressure (760 mm Hg at sea

level), P_{H2O} is the partial pressure of water in humidified air (47 mm Hg), and the RQ is the ratio of CO_2 production to oxygen consumption. The RQ in most people is 0.8.

Simplified for a patient breathing room air (FiO_2 of 21%), the equation reads

$$P_AO_2 = 150 - 1.2(PaCO_2)$$

For a normal $PaCO_2$ of 40 mm Hg, the P_AO_2 should be 102 mm Hg.

Normally, there is a small difference between the partial pressure of oxygen in the alveoli and that seen in arterial blood (the PaO_2). This is called the A-a gradient, and it represents the small fraction of blood that doesn't participate in gas exchange because of bronchopulmonary anastomoses. The normal gradient is less than 10 mm Hg, but this increases with age. It can also increase with supplemental oxygen. The predicted A-a gradient while breathing 100% oxygen can be as high as 110 mm Hg.

Why is this important? Well, go back to your basic chemistry. The partial pressure of all of the gases in the alveolar space can only add up to the total pressure of the air. Therefore, if the $PaCO_2$ is elevated, the P_AO_2 has to go down. Only so many marbles in the jar, so to speak. If the P_AO_2 goes down, the PaO_2 falls as well. Hypoxemia can be due solely to hypercarbia if the $PaCO_2$ gets high enough, and *a normal A-a gradient means that that there is no problem with the lungs or the pulmonary circulation.* The hypoxemia is a result of inadequate ventilation alone (pure Type II respiratory failure). If the A-a gradient is widened, then there must be some venous admixture. The three mechanisms of venous admixture are shunt, dead space, and VQ mismatch.

Shunt

Shunt is easy to visualize—blood passing from the right side of the heart to the left side of the heart through areas where there is no ventilation

whatsoever. The V/Q ratio is zero. A shunt can be intracardiac or intrapulmonary. The gas exchange abnormality with shunt is profound hypoxemia with preserved ventilation. The $PaCO_2$ doesn't begin to rise until the shunt fraction exceeds 40-50% of the pulmonary blood flow. The normal shunt fraction is less than 3%.

Intracardiac shunts in adults include uncorrected atrial septal defects and ventricular septal defects. The Eisenmenger Syndrome is a VSD with shunt reversal (it begins left-to-right, but as the right ventricle hypertrophies the shunt becomes a right-to-left one and the patient becomes hypoxemic).

Pulmonary shunts are caused by something preventing inspired gas from reaching alveoli. Examples include atelectasis, ARDS, pulmonary edema, and consolidation from pneumonia.

Shunt is characterized by hypoxemia resistant to correction. As the shunt fraction increases, the hypoxemia will get worse despite breathing high levels of oxygen. With a shunt fraction of 50%, even the administration of 100% oxygen will rarely take the PaO_2 above 60 mm Hg.[2] Therefore, the treatment of hypoxemic respiratory failure resulting from a shunt requires more than supplemental oxygen. Positive pressure ventilation to recruit and stabilize collapsed lung units is required.

The shunt fraction can be calculated if the mixed venous oxygen content can be sampled using a pulmonary artery catheter (see Appendix for the equation). This has to be done with the patient breathing 100% oxygen to eliminate the contribution of VQ mismatch to the hypoxemia. Because the equation is cumbersome and requires invasive testing, it's useful to have a shortcut. The P/F ratio is calculated by dividing the PaO^2 by the FiO_2. For example, say a patient has a PaO_2 of 100 mm Hg on 60% oxygen. His P/F ratio is 100/0.6, or 167. A P/F ratio less than 200 suggests a shunt fraction greater than 20%.

VQ Mismatch

Normal cardiac output is 5 L/min. Normal minute ventilation (rate × tidal volume) is 4 L/min. The average ventilation-perfusion ratio, then, is 4/5 or 0.8. As the metabolic demands of the body increase, cardiac output and minute ventilation increase accordingly. Areas that are poorly ventilated don't get much blood flow, though, because of hypoxic pulmonary

vasoconstriction.

In every other organ system, hypoxia results in vasodilatation. In the lungs, however, alveolar hypoxia causes vasoconstriction. This is a good thing—why send blood to lung units that don't have a whole lot of oxygen to drop off to the red blood cells? When this balance is lost, VQ mismatch occurs and leads to hypoxemia. This is also the reason why patients with COPD and chronic CO_2 retention get a respiratory acidosis when someone gives them high levels of oxygen.

Certain disease states can alter airway caliber and tone and affect gas delivery to the alveoli, which results in lung units which are more perfused than ventilated—a VQ ratio less than 0.8. Examples of this are asthma, COPD, interstitial lung disease, tracheobronchitis, and pneumonitis. Other diseases may impede proper blood flow to ventilated units, causing more ventilation than perfusion and a VQ ratio of more than 0.8. This can be seen with chronic thromboembolic disease, vasculitis, and overdistension of alveoli during positive pressure ventilation. Patients who are supine and are on a ventilator have VQ mismatch owing to the air going anterior and the blood going posterior due to gravity.

VQ mismatch is the most common cause of hypoxemic respiratory failure and usually corrects readily with supplemental oxygen. Even severe cases of VQ mismatch are responsive to breathing 100% oxygen. Inability to correct the PaO_2 with high levels of oxygen suggests a shunt.

Dead Space Ventilation

Dead space is the opposite of shunt—the alveoli are ventilated but there is absolutely no perfusion. The VQ ratio is ∞. Dead space is seen with large pulmonary embolism, venous air embolism, and low cardiac output. It can also be seen with significant overdistension of alveoli during positive pressure ventilation and dynamic hyperinflation in patients with COPD. The gas exchange abnormality seen with dead space ventilation is both hypoxemia and hypercarbia. The CO_2 is not cleared because the venous blood never comes in contact with alveoli.

Remember that everyone has anatomic dead space, which refers to the trachea and large airways that hold air but don't participate in gas exchange. This is usually 150-180 mL, about 1 mL for every cm in height. This volume is part of the minute ventilation and should account for less than 30% of the

tidal volume ($V_D/V_T \leq 0.3$). Rapid shallow breathing can increase the proportion of the minute volume that is dead space.

For example, a patient with a tidal volume of 500 mL has an anatomic dead space of 150 mL and a V_D/V_T ratio of 0.3. His respiratory rate is 12, for a minute volume of 6 L/min (of which 1.8 L is wasted dead-space ventilation and 4.2 L is alveolar ventilation). If his respiratory rate increases to 30 and his tidal volume drops to 200 mL, he still has the same minute volume of 6 L/min. His dead space is still 150 mL per breath, though, which means that 4.5 L/min (30 × 150 mL) of his minute ventilation is wasted, leaving only 1.5 L/min for alveolar ventilation. His V_D/V_T ratio is now 0.75. In this case, the $PaCO_2$ would rise and the PaO_2 would fall due to alveolar hypoventilation.

Tachypnea and labored respirations with a normal $PaCO_2$ usually indicate increased dead space and a relative alveolar hypoventilation. This is one of the earliest signs of impending respiratory failure. It is nearly impossible to determine the $PaCO_2$ with any kind of accuracy by clinical exam, so arterial blood gas measurements are essential.

Hypoxemia vs. Hypoxia

Hypoxemia refers to a PaO_2 less than 60 mm Hg. Hypoxia refers to inadequate delivery of oxygen to tissues or ineffective cellular utilization of oxygen, leading to anaerobic metabolism. It’s possible to be hypoxemic but not hypoxic, and it’s also possible to be hypoxic but not hypoxemic. Of course, you can be hypoxemic and hypoxic, or neither hypoxic nor hypoxemic. Clear enough?

To better understand this, we have to consider how oxygen is delivered to the tissues. Oxygen is bound to hemoglobin and carried to the capillary beds, where it is unloaded into the cellular milieu; the deoxygenated hemoglobin then picks up CO_2 and takes it back to the lungs to be excreted. Since 97% of the oxygen in the bloodstream is bound to hemoglobin, it makes more sense to focus on the percentage of hemoglobin saturated with oxygen than the partial pressure of oxygen in plasma.

Oxygen Content Equation

$$CaO_2 = 1.34\ (Hgb)\ (SaO_2) + 0.003(PaO_2)$$

where CaO_2 is the content of oxygen in arterial blood, expressed in mL O_2/dL blood; Hgb is in g/dL; SaO_2 is the arterial saturation of oxygen; and PaO_2 is the partial pressure of oxygen in plasma.

For a normal person with hemoglobin of 15 g/dL, SaO_2 of 100%, and PaO_2 of 100 mm Hg, the CaO_2 is 20.4 mL O_2/dL blood. The oxygen dissolved in plasma contributes 0.3 mL O_2, or less than 1.5% of the total.

Oxygen delivery is the CaO_2 multiplied by the cardiac output. It's necessary to multiply this by 10, since CaO_2 is measured in deciliters and cardiac output is measured in liters. A normal person with a cardiac output of 5 L/min has an oxygen delivery (DO_2) of 1020 mL O_2/min. Looking at the above equations, you can see that the most important factors governing oxygen delivery are the cardiac output, hemoglobin content, and the arterial oxygen saturation. The PaO_2 plays a minor role.

Four Types of Hypoxia

Hypoxemic: low SaO_2 leading to low delivery of O_2 to the tissues.

Stagnant: low cardiac output, which leads to tissue hypoxia even if the patient is breathing 100% oxygen.

Anemic: not enough red blood cells to carry oxygen to the tissues.

Cytopathic: the heart pumps enough oxygen to the tissues, but something inhibits effective oxidative phosphorylation

(septic shock, cyanide poisoning, salicylate poisoning).

Hypercarbic Respiratory Failure

Type II, or hypercarbic*, respiratory failure is due to an inability of the body to clear CO_2. Hypoxemia may occur due to hypoventilation, but this is correctable with supplementary oxygen. The best way to determine the cause of hypercarbic respiratory failure is to consider the various ways the body controls CO_2 elimination and look for breakdowns in the system.

Normally, the body is very good at maintaining a normal $PaCO_2$. Even during deep sleep, the $PaCO_2$ varies by 2-3 mm Hg at most. This balance is maintained by the respiratory centers in the medulla oblongata, which stimulate diaphragmatic contractions via the phrenic nerve. When acute hypercarbic respiratory failure occurs, the problem can be localized to either the signaling pathways of the nervous system or the bellows of the respiratory system. Ask yourself—*where is the problem?*

Localizing the Cause of Hypercarbia

Brainstem: drug overdose, trauma, intracerebral or subarachnoid hemorrhage, infection, obesity hypoventilation syndrome, hepatic or uremic encephalopathy, bulbar poliomyelitis?

Spinal Cord: lesion at C4 or higher, central cord hematoma, traumatic injury, “high spinal” anesthesia, polio, epidural abscess, transverse myelitis?

Peripheral Nerves: phrenic nerve paralysis, tick paralysis, acute inflammatory demyelinating polyneuropathy (Guillain-Barré syndrome), acute intermittent porphyria, heavy metal poisoning?

Neuromuscular Junction: botulism, myasthenia gravis, paraneoplastic syndrome, neuromuscular blocking drugs?

Muscles: muscular dystrophy, polymyositis, dermatomyositis, hypothyroidism, hypokalemia, hypophosphatemia, hypermagnesemia, steroid-induced myopathy, critical illness polymyopathy?

Thoracic Cage: kyphoscoliosis, thoracoplasty, morbid obesity, flail chest, abdominal compartment syndrome, ankylosing spondylitis, circumferential burn?

Lungs: COPD? Dynamic hyperinflation?

Upper Airway Obstruction

Obstruction of the upper airway can cause respiratory failure. Common causes of upper airway obstruction requiring acute treatment are trauma, infection (peritonsillar abscess, retropharyngeal abscess), inhaled foreign body, inhalational injury, and angioedema. Stridor is a sign of airflow obstruction at or above the glottis, while expiratory wheezing usually indicates obstruction of the lower airways. Intubation should always be considered, preferably before the patient makes it clear that his airway is completely obstructed.

Metabolic Control

CO_2 is the major byproduct of cellular metabolism. While hypercarbia is most often due to one of the disorders of ventilatory control, occasionally CO_2 production can exceed the capacity of the respiratory system. This can occur during thyroid storm, malignant hyperthermia, cyanide or salicylate poisoning, and with massive catabolism. Ventilatory support may be needed.

Hemodynamic instability and shock can also lead to respiratory failure due to the hypermetabolism seen with sepsis, trauma, and burn injuries. Blood that is directed toward the diaphragm and accessory muscles is shunted away from the splanchnic and hepatic circulation, which can lead to lactic acidosis. Excessive work of breathing can also worsen myocardial ischemia. A worsening metabolic acidosis or cardiac ischemia in the setting of shock are signs of impending respiratory failure and justify mechanical ventilatory

support.

A crucial part of managing acute respiratory failure in a patient with a severe metabolic acidosis is to provide enough minute ventilation to compensate for the metabolic process. If a man with ischemic bowel has bicarbonate of 4 and requires intubation, the minute ventilation should be set high enough to obtain a $PaCO_2$ of 14 mm Hg, the expected amount of respiratory compensation. If the ventilator is set so that the $PaCO_2$ is in the "normal" range of 35-45, the pH will plummet, and the patient could arrest.

Treatment of Acute Respiratory Failure

The most important thing is to find and treat the underlying cause, if possible. Support can be given to the patient during the workup and treatment and should not be delayed. Noninvasive support measures include supplemental oxygen and inhaled bronchodilators. Positive pressure ventilation can be given via a noninvasive mask system like CPAP or BiPAP —these are particularly effective for COPD exacerbations with hypercarbia and cardiogenic pulmonary edema. More severe manifestations of respiratory failure like ARDS, multilobar pneumonia, neuromuscular diseases, and cardiogenic shock usually require intubation and mechanical ventilation.

With the exception of reducing the shunt fraction with positive end expiratory pressure, mechanical ventilation is not a therapeutic intervention. The goal of ventilation is to simply maintain adequate gas exchange and metabolic function while the underlying disease process either gets treated or (more commonly) resolves on its own. Thus, the physician should focus on treating reversible causes of respiratory failure and minimizing further injury to the patient. When the patient is ready to come off the ventilator, he'll let you know.

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* In the future, patients can be plugged into a machine that will immediately analyze all of their medical problems and print out a list for the physician. I saw that on Star Trek. Until then, we still have to do an H&P.

* Alternatively called hypercapnic

Chapter 5
Oxygen Delivery and Consumption

Many textbooks on respiratory and critical care medicine begin with statements like, “Oxygen is the most necessary and basic building block of life.” In clinical training, the early application of high-flow oxygen is taught as a life-saving maneuver in emergencies. In the emergency department and intensive care unit, much importance is placed on keeping the pulse oximeter reading over 90% (and usually over 95%); likewise, there is a compulsion to keep the PaO_2 in the normal range of 90-100 mm Hg.

At first glance, there is nothing wrong with this approach. Oxygen is indeed necessary for life, and avoiding hypoxemia is a core part of resuscitation. When treating patients with severe respiratory failure, however, attaining a normal PaO_2 may be either impossible, or only possible by the application of injurious airway pressures. Therefore, a more complete understanding of oxygen delivery and consumption is necessary.

Oxygen Content

Each gram of hemoglobin can bind 1.34 mL of oxygen when fully saturated. A small amount of oxygen is also carried in the plasma in its dissolved form. This is represented by the PaO_2. The solubility coefficient for oxygen in plasma is 0.003. Putting all of this together yields the oxygen content equation:

$$\mathbf{CaO_2 = 1.34 \times Hgb \times SaO_2 + [PaO_2 \times 0.003]}$$

With normal hemoglobin of 15 g/dL, SaO_2 of 100%, and a PaO_2 of 100

mm Hg, the oxygen content of arterial blood is 20.4 mL O_2/dL blood. It is important to note that the contribution made by the dissolved oxygen (PaO_2 x 0.003) is very small—0.3 mL O_2/dL blood. The hemoglobin binds 98.5% of the oxygen content. The fraction contributed by the dissolved oxygen is negligible. If the FiO_2 on the ventilator were increased to bring the PaO_2 up to 500 mm Hg (keeping the SaO_2 at 100%), only 1.2 mL O_2/dL blood would be added to the oxygen content.

Keeping the PaO_2 elevated beyond what's necessary for adequate saturation of the hemoglobin is unlikely to be consequential except in cases of profound anemia (Hgb < 5 g/dL) or hyperbaric conditions. In fact, the PaO_2 can often be ignored when calculating oxygen content and delivery in order to make the math easier. This leads us to the first rule of oxygen: *the SaO_2 is what matters, not the PaO_2.*

Oxygen Delivery

Once the arterial blood is loaded with oxygen, it is delivered to the tissues to be used for metabolism. The amount of blood circulated per minute is the cardiac output, which is expressed in liters blood per minute. Since the CaO_2 is measured in deciliters, the units are converted by multiplying by 10. This yields the oxygen delivery equation:

$$\mathbf{DO_2 = CO \times CaO_2 \times 10}$$

If a normal cardiac output is 5 L/min, the DO_2 is 1020 mL O_2/minute. In order to make comparisons among different patients of various heights and weights, this can be indexed by dividing the DO_2 by the body surface area. A "typical" body surface area is 1.7 m^2, so the "typical" DO2I would be 1020/1.7, or 600 mL O_2/min/m^2.

The cardiac output has the greatest influence on oxygen delivery. Even during periods of arterial hypoxemia, an increase in cardiac output can be sufficient to deliver the necessary amount of oxygen to the tissues. The table below shows the effect that an increase in cardiac output can have on oxygen

delivery, even with significant anemia or hypoxemia. It also shows that anemia has a more pronounced effect on oxygen delivery than hypoxemia. For the purposes of simplifying the calculations, the PaO_2 has been omitted. This leads us to the second rule of oxygen: *an increase in cardiac output can offset hypoxemia.*

Effect of Different Variables on Oxygen Delivery

CO	**Hgb**	**SaO_2**	**DO_2**
5 L/min	15 g/dL	100%	1005
8 L/min	7 g/dL	100%	750
8 L/min	15 g/dL	75%	1206
3 L/min	15 g/dL	100%	603

Oxygen Consumption

During periods of rest, the body's consumption of oxygen (VO_2) is approximately 200-250 mL O_2/minute. Indexed for body surface area, the resting VO_2I is 120-150 mL O_2/min/m2. Normal subjects can increase their VO_2 during peak exercise by a factor of 10, and elite athletes can reach a maximum VO_2 of 20-25 times their resting consumption. During critical illnesses like septic shock, multisystem trauma, or burn injury, VO_2 increases over baseline by approximately 30-50%.

The consumption of oxygen by the tissues (VO_2) varies by organ system. The brain and heart consume the most delivered oxygen, while hair, bones, and nails consume a negligible amount. This can be further complicated by the fact that different organ systems receive different amounts of the cardiac output—the brain consumes the most oxygen, for example, but also receives

15% of the total blood flow. The coronary circulation, on the other hand, accounts for only 5% of the total cardiac output so the percentage of delivered oxygen that is consumed is much higher. Fortunately for the clinician, this is not important because regional monitoring of oxygen delivery and consumption is practical only in laboratory animals. Measurement of the total body VO_2, on the other hand, can be done rather easily with a pulmonary artery catheter (more accurate) or by using a combination of a noninvasive cardiac output monitor along with a measurement of central venous oxygen saturation (less accurate). While this is not as precise as directly measuring the content of oxygen in expired gas, it is a close enough approximation for clinical use.

By measuring the mixed venous oxygen saturation in the pulmonary artery, the venous oxygen content can be calculated:

$$\mathbf{CvO_2 = 1.34 \times Hgb \times SvO_2 + [PvO_2 \times 0.003]}$$

As with the arterial oxygen content equation, the minor contribution made by the dissolved oxygen (in this case, the PvO_2), can be omitted from the calculation. Thus, for a hemoglobin of 15 g/dL and a normal SvO_2 of 75%, the venous oxygen content is 15.1 mL O_2/dL blood. The difference between arterial and venous oxygen content is normally 3-5 mL O_2/dL blood.

The VO_2 can then be calculated by multiplying the arterial-venous oxygen difference by the cardiac output and converting units:

$$\mathbf{VO_2 = CO \times [CaO_2 - CvO_2] \times 10}$$

Expanded, this equation is:

$$\mathbf{VO_2 = CO \times [(1.34 \times Hgb \times SaO_2) - (1.34 \times Hgb \times SvO_2)] \times 10}$$

Rearranged (and simpler):

$$VO_2 = CO \times 1.34 \times Hgb \times (SaO_2 - SvO_2) \times 10$$

In this case, with a cardiac output of 5 L/min, the DO_2 is 250 mL O_2/minute. Indexed for a typical body surface area of 1.7 m2, the DO2I is 147 mL O_2/min/m2.

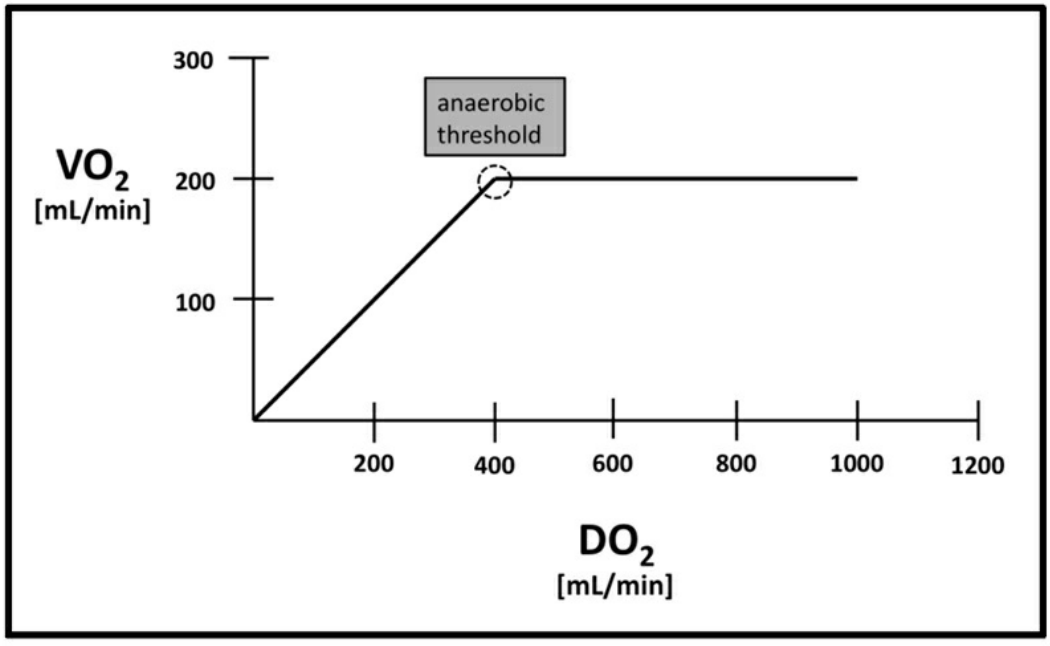
Using the DO_2 and VO_2 Together

Knowing the DO_2 or VO_2 in isolation is not particularly useful. The clinical question is whether the delivery is adequate to meet the body's consumption requirements. To answer this, the DO_2:VO_2 ratio is helpful. During periods of both rest and exercise, the DO_2:VO_2 ratio is maintained at approximately 4:1 to 5:1 by changes in the cardiac output. This provides a reserve of sorts— after all, it wouldn't be very useful from a survival perspective to only deliver as much oxygen as the body absolutely needs at any given time. This lack of a physiologic reserve would mean that a person would have no ability to withstand a sudden change in circumstances like having to sprint away from an attacker, or deal with a high fever or pulmonary embolism.

As seen in the following figure, the DO_2 can vary widely as the VO_2 remains constant. This reflects the aforementioned physiologic reserve. As the DO_2 declines, however, it can reach a point at which further drops in oxygen delivery cause a fall in consumption. This point is known in physiology as the hypoxic, or anaerobic, threshold. It is at this point that the reserve is exhausted, and the consumption becomes supply dependent. A patient at or below this point for any kind of prolonged period will become severely acidotic and, in most cases, will not survive.

It would make sense that the anaerobic threshold would occur when the DO_2 equals the VO_2. Experimentally, however, it has been shown that the threshold is closer to the 2:1 mark and is explained by the variable oxygen consumption of different organ systems. Cardiac output delivered to hair, teeth, and bones doesn't contribute much to meet the needs of the more vital organ systems.

DO_2:VO_2 Relationship



Mathematically, the DO_2:VO_2 ratio looks like this:

$$DO_2:VO_2 = \frac{CO \times 1.34 \times Hgb \times SaO_2 \times 10}{CO \times 1.34 \times Hgb \times (SaO_2 - SvO_2) \times 10}$$

Cancelling common factors greatly simplifies the equation:

$$DO_2:VO_2 = \frac{\cancel{CO \times 1.34 \times Hgb \times} SaO_2 \cancel{\times 10}}{\cancel{CO \times 1.34 \times Hgb \times} (SaO_2 - SvO_2) \cancel{\times 10}}$$

$$DO_2:VO_2 = \frac{SaO_2}{(SaO_2 - SvO_2)}$$

If the SaO_2 is assumed to be 100%, then the SvO_2 correlates with the DO_2:VO_2 ratio:

DOv_2:VO_2	SvO_2
5:1	**80%**
4:1	**75%**

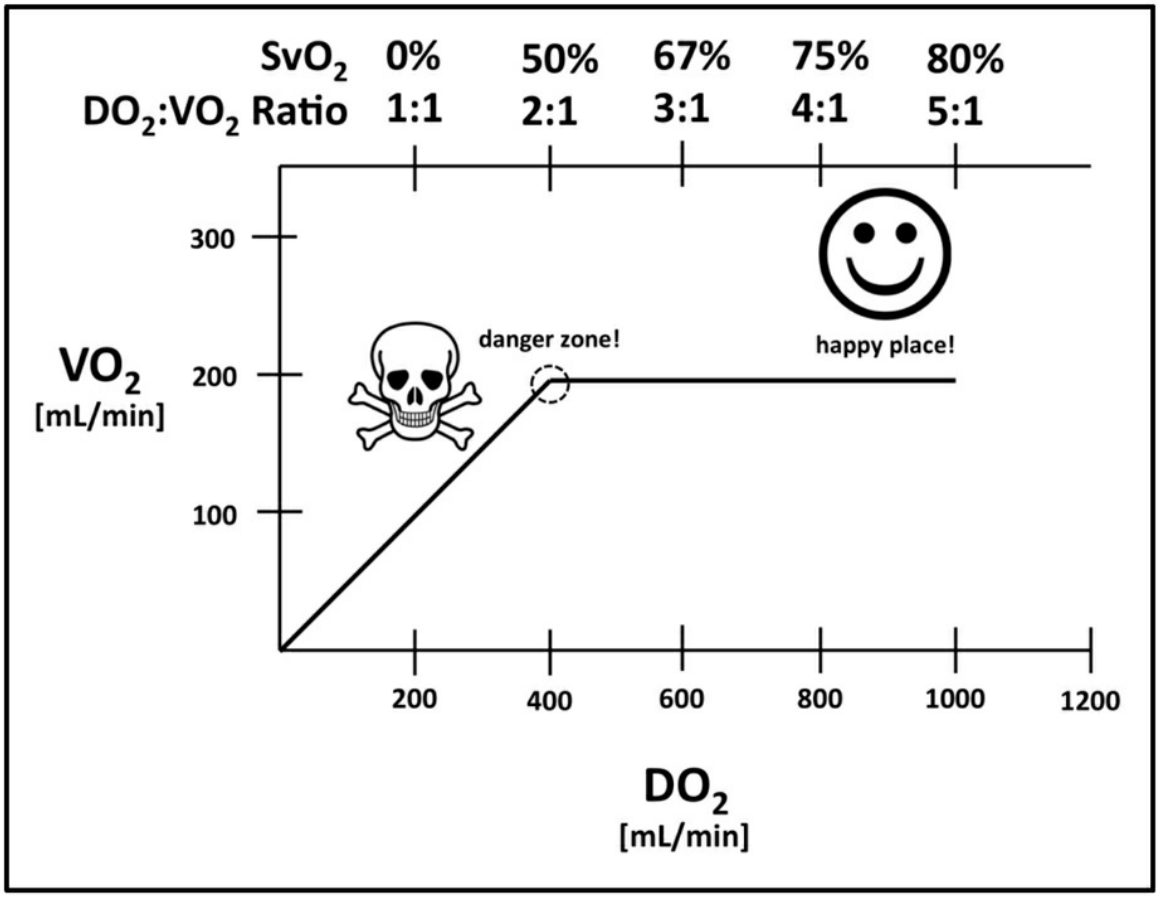
3:1	**67%**
2:1	**50%**

This correlation makes clinical estimation of the DO_2:VO_2 relationship much easier, as the SvO_2 can be measured directly and continuously by a pulmonary artery catheter. If a pulmonary artery catheter is not present, a central venous oxygen saturation (ScvO2) can be measured by obtaining a venous blood gas from a central venous line placed in the internal jugular or subclavian vein. The ScvO2 is usually 5-8% higher than the SvO_2. While not as accurate as the true mixed venous oxygen saturation obtained with a pulmonary artery catheter, the ScvO2 can be used to estimate of the DO_2:VO_2 relationship.

The SvO2, as a surrogate for the DO_2:VO_2 relationship, can be used to identify when a patient has insufficient oxygen delivery to meet consumption requirements. The SvO_2 also has the advantage of not requiring continuous calculation of the actual DO_2 and VO_2— any changes in the relationship between delivery and consumption will be reflected in the SvO_2. The SvO_2 drops as oxygen delivery drops relative to consumption. An SvO_2 below 70% should warrant evaluation, and an SvO_2 below 60% is definitely concerning —it means that the patient is approaching the anaerobic threshold.

Looking back at the DO_2 equation, impaired oxygen delivery is always due to either low cardiac output, anemia, or hypoxemia. Correction of these should increase DO_2, with a resultant increase in SvO_2. Keep in mind that the cardiac output has the most significant effect on DO_2, and conditions like congestive heart failure, hypovolemia, hemorrhagic shock, and cardiac tamponade will all reduce cardiac output. This leads us to the third rule of oxygen: *the SvO_2 is low in low-flow states.*

Using the SvO_2 With DO_2 and VO_2



Patients with severe respiratory failure may have uncorrectable hypoxemia. A reduction in the SaO_2 will lead to a corresponding reduction in SvO_2 if the DO_2:VO_2 ratio remains constant. Calculating the oxygen extraction ratio is a quick way to estimate the balance between oxygen delivery and consumption even when the SaO_2 is markedly reduced:

$$O_2ER = \frac{SaO_2 - SvO_2}{SaO_2}$$

For a normal SaO_2 of 100% and SvO_2 of 75%, the O_2ER is: (1.0– 0.75)/1.0 = 0.25/1.0 = 0.25, or 25%. This means that of the delivered oxygen, 25% was extracted and consumed by the tissues. A normal O_2ER is 20-25%.

As an example, consider a patient with severe respiratory failure whose SaO_2 is 84%. His SvO_2 is 60%. According to the above figure, an SvO_2 this low would be concerning. However, the assumption in Figure 2 is that the SaO_2 is 100%. Calculating the oxygen extraction ratio:

$$O_2ER = (0.84 – 0.60)/0.84 = 0.24/0.84 = 0.286, \text{ or } 28.6\%$$

While this is a bit higher than the normal range of 20-25%, it isn't that much. Put another way, this indexing of the oxygen extraction would correlate with an SvO_2 of 71.4% (if the SaO_2 were 100%).

As a second example, take a patient with severe respiratory failure with an SaO_2 of 86%. His SvO_2 is 49%. The O_2ER is (0.86 – 0.49)/0.86, or 43%. This would correlate with an SvO_2 of 57% if the SaO_2 were 100% and is certainly concerning for a low cardiac output state. An O_2ER of 30% or higher should warrant investigation, and an O_2ER higher than 40% indicates that the patient is approaching the anaerobic threshold.

The fourth rule of oxygen: *the DO_2:VO_2 ratio, SvO_2, and O_2ER reflect the balance between delivery and consumption. They don't represent a specific target for intervention.*

So, How Much Oxygen Is Really Needed?

Unfortunately for physiologists and writers of clinical algorithms, simply saying to keep the SvO_2 over 70% and all will be well doesn't work. This should come as no surprise to anyone familiar with the medical literature in critical care medicine— multiple studies proposing one physiologic manipulation, or another have been consistently disproven. The combined processes of oxygen delivery, oxygen consumption, stress response, and cellular adaptation are far too complex to be summed up in this chapter, let alone a one-size-fits-all algorithm.

A normal PaO_2 while breathing ambient air at sea level is 90100 mm Hg, but humans are able to tolerate much less over prolonged periods of time. The minimum necessary PaO_2 and SaO_2 is not known, and it is unlikely that any IRB will grant approval to a study aiming to withhold supplemental oxygen from critically ill patients. The degree of tolerable hypoxemia is also

highly variable, and depends on factors such as the patient's age, comorbid conditions, living environment, genetic factors, and ability to cope with physiologic stress. What is known is that some people are able to survive moderate and even severe hypoxemia. Keep the following in mind:

- Mitochondrial PO_2 in cardiac and skeletal muscle is normally between 1 and 5 mm Hg.
- Oxidative phosphorylation in mitochondria doesn't begin to fail until the PO_2 is between 0.1 and 1 mm Hg.
- Climbers on Mount Everest who obtained femoral arterial samples from each other had PaO_2 in the 24-28 mm Hg range and lived to tell the tale.
- In septic shock, the problem is not inadequate oxygen delivery. It's the inability of the tissues to properly metabolize the delivered oxygen. That's why patients die despite having an SvO_2 of 80%. The reasons for this are (very) incompletely understood.
- In the various ARDSNet trials, a PaO_2 as low as 55 mm Hg (with an SaO_2 of 88%) was considered acceptable. This is probably the best we will get as far as prospective evidence on the subject.
- Patients in the ARDSNet trial who received higher tidal volumes had better oxygenation, but also had a higher mortality rate. This suggests that preventing lung injury was more important than improving oxygenation.
- Many interventions have been shown to improve oxygenation in mechanically ventilated patients, but not to improve survival.

Using lactate levels is an appealing method of determining whether oxygen delivery is adequate, but it has its limitations as well. Most lactate production in critical illness is not due to anaerobic metabolism, despite common assumptions. Instead, it is a product of increased pyruvate production (with metabolism to lactate) in the setting of impaired or altered glycolysis and gluconeogenesis. Lactate is the preferred fuel for cardiac myocytes in the setting of adrenergic stimulation and is produced by aerobic

cellular respiration. Thus, lactate should be viewed as a nonspecific marker of physiologic stress. If the lactate comes down following intubation, fluid resuscitation, etc., then it simply indicates that the patient is responding to therapy. It doesn't imply restoration of aerobic metabolism in previously anaerobic tissues. Likewise, an increasing lactate may indicate that the patient has a condition that is leading to an increase in sympathetic tone and cortisol-mediated stress response. Increasing oxygen delivery may or may not help the situation—it depends on what the underlying condition is.

This concept leads to the fifth rule of oxygen: *SaO_2, SvO_2, O_2ER, and lactate are all pieces of information and not goals in themselves.* They must be taken into account along with urine output, peripheral perfusion, mentation, and other clinical information before any treatment decisions can be made.

Oxygen Toxicity

The idea that supplemental oxygen can be toxic, especially in high doses, is not new. In neonates, high FiO_2 has been associated with retinopathy and bronchopulmonary dysplasia. In adults, there is evidence of worse outcomes with hyperoxia in the setting of acute myocardial infarction and following cardiac arrest. High FiO_2 in adults can cause irritation of the tracheobronchial tree and absorption atelectasis (due to the oxygen being absorbed without the stabilizing effect of nitrogen gas, leading to alveolar collapse). This is discussed in more detail in the chapter on "Safety Limits and Lung Protection." The bottom line is that avoiding hyperoxia is easy and can be accomplished by reducing the FiO2. Even normoxia may not be necessary, and it may be prudent to tolerate a degree of permissive hypoxemia in order to avoid exposing the patient to high FiO_2 or ventilator pressures. Remember that cardiac output has a much more significant effect on oxygen delivery than the saturation and focus on signs of adequate or inadequate oxygen delivery rather than strictly following the SaO_2 and PaO_2. This approach leads us to the sixth and final rule of oxygen: *give the patient just as much oxygen as he needs. This may be less than you think.*

Six Rules of Oxygen

1. **The SaO_2 is what matters, not the PaO_2.**
2. **An increase in cardiac output can offset hypoxemia.**
3. **The SvO_2 is low in low-flow states**
4. **The DO_2:VO_2 ratio, SvO_2, and O_2ER reflect the balance between delivery and consumption. They don't represent a specific target for intervention.**
5. **SaO_2, SvO_2, O_2ER, and lactate are all pieces of information and not goals in themselves. They must be taken into account along with urine output, peripheral perfusion, mentation, and other clinical information before any treatment decisions can be made.**
6. **Give the patient just as much oxygen as he needs. This may be less than you think.**

Chapter 6
Permissive Hypercapnia

Permissive hypercapnia is the practice of allowing a mechanically ventilated patient to develop or remain in a respiratory acidosis rather than exposing him to the risk of injurious ventilator settings. For the purposes of this chapter, permissive hypercapnia is defined as a $PaCO_2$ > 45 mm Hg with a pH < 7.35. Hickling et al. first described this concept in two papers that demonstrated a survival benefit with lower tidal volumes and elevated $PaCO_2$ levels.[3,4] This work was influential on later studies that showed the superiority of low tidal volume ventilation, including the landmark ARMA study performed by the ARDS Network investigators. Most of the studies examining this topic have focused on the benefit of using a lower tidal volume (4-6 mL/kg predicted body weight) in ARDS. There is less research on the benefits and risks of permissive hypercapnia itself, but there may be some advantages to permitting a mild to moderate respiratory acidosis in patients with severe respiratory failure.

Pulmonary Benefits of Permissive Hypercapnia

The primary rationale for hypercapnia is that avoiding iatrogenic ventilator-induced lung injury is more important that attaining normal gas exchange. Overdistension of healthy alveoli leads to cellular injury and is referred to as volutrauma. This is the primary mechanism of ventilator-induced lung injury (VILI) and is independent of distending pressures (barotrauma). The ARMA study demonstrated a reduction in mortality in patients with ARDS when tidal volumes of 4-6 mL/kg PBW were used, compared with tidal volumes of 12 mL/kg.[5] This benefit was seen despite worsening gas exchange in the low tidal volume group. In patients with status asthmaticus, using lower tidal volumes and respiratory rates prevents

dynamic hyperinflation, pneumothorax, and pneumomediastinum, even though it may lead to a respiratory acidosis. Permissive hypercapnia is considered acceptable because the benefits of avoiding lung injury are considered far more important than achieving “normal” alveolar ventilation.

Since current practice emphasizes the use of a low tidal volume in ARDS, increasing the tidal volume to correct a respiratory acidosis is seldom done. Instead, the respiratory rate is adjusted to increase or decrease the minute ventilation. Most of the time, increasing the respiratory rate on the ventilator is sufficient to blow off CO_2 and normalize the pH. This may not be necessary, however, as patients are able to tolerate even a significant respiratory acidosis so long as oxygenation is maintained.[6] In fact, there may be harm with this common practice. An increase in the frequency of tidal ventilation invariably leads to an increase in the cyclical opening and closure of vulnerable lung units. A patient with a set respiratory rate of 20 breaths per minute will have 11,520 more ventilatory cycles per day than another patient with a respiratory rate of 12 breaths per minute. Each one of those ventilatory cycles has the potential, albeit small, to contribute to VILI. Laboratory data supports the idea of using a lower ventilator rate whenever possible;[7] however, prospective studies in humans will be needed to validate this concept. In the absence of data, though, it is certainly reasonable to question the necessity of routinely increasing the ventilator rate to correct mild to moderate acidemia.

Extrapulmonary Benefits of Permissive Hypercapnia

No prospective, randomized human trials examining the extrapulmonary benefits of permissive hypercapnia have been done. There are several laboratory studies in animals that have demonstrated a beneficial effect of hypercapnia on free radical production, myocardial injury, and cerebral ischemia.[8] This reduction in pro-inflammatory cytokines and oxidative injury may prove to be helpful in reducing multisystem organ dysfunction, especially because the majority of patients with ARDS die of multisystem organ failure rather than of primary respiratory failure.

In healthy human volunteers, controlled hypercapnia under general anesthesia was shown to increase both cardiac output and tissue oxygenation.[9] A study of patients with severe ARDS demonstrated an

increase in cardiac output and systemic oxygen delivery with a tidal volume reduction and hypercapnic acidosis;[10] the same study, however, also showed worsening right ventricular function and hemodynamics. In a study of patients with subarachnoid hemorrhage and cerebral vasospasm, controlled hypercapnia led to an increase in cerebral blood flow without prohibitory elevations in intracranial pressure.[11] While this is not sufficient to justify a change in recommended ventilator management, these findings do argue against the presumption of harm with respiratory acidosis during mechanical ventilation.

Buffering

In the ARMA study and subsequent ARDS Network studies, administration of buffering fluids was permitted to keep the pH ≥ 7.15. Sodium bicarbonate ($NaHCO^3$) is often used to treat acidemia, but it does have several drawbacks. Under usual conditions, the bicarbonate anion is converted to CO_2 and H_2O via carbonic anhydrase:

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

The elimination of the excess CO_2 produced by this reaction is not normally an issue—one or two breaths are sufficient to clear it. In the setting of severe respiratory failure, however, elimination of the CO_2 may not be possible, and the pH may in fact fall with the administration of sodium bicarbonate. In addition, CO_2 diffuses freely over cell membranes (including in the CSF), but HCO_3- does not. This has the effect of worsening intracellular acidosis, even if the systemic pH rises. A transient hemodynamic improvement is often seen when a bolus of sodium bicarbonate (e.g., an “amp”) is given, but this is more likely due to the loading of sodium than the change in pH—similar effects are seen with bolus dosing of hypertonic saline. Keep in mind that the $NaHCO_3$ given in a 50 mL ampule is 8.4%, which is a very hypertonic sodium solution.

THAM (tris-hydroxymethyl aminomethane) is a direct H^+ ion buffer that does not depend on alveolar ventilation like $NaHCO_3$. It also crosses cell membranes freely and produces intracellular buffering. This may be a more

effective buffer for hypercapnic acidosis, but there are scant clinical data for its efficacy. At the time of this writing, the point is moot—THAM has been discontinued by the only manufacturer that was producing it.

The necessity for buffering a respiratory acidosis during mechanical ventilation is debatable. The purported benefits of permissive hypercapnia (beyond the prevention of volutrauma) may be lost when the pH is increased. Administration of sodium bicarbonate may have some adverse effects, as described above, and there are no available non-bicarbonate buffers available for clinical use. Additionally, acidemia may confer a protective effect on hepatic and renal function, and systemic acidosis shifts the oxygen-hemoglobin dissociation curve rightward, thereby augmenting tissue oxygen delivery. Using buffer therapy to keep the pH ≥ 7.15 is a common, but unproven, practice. Until clinical studies show a benefit to doing this, it would be prudent to reserve buffering for situations where the clinician feels that the acidosis is having an adverse effect on the patient.

Downsides of Permissive Hypercapnia

Despite the aforementioned benefits, there are some clinical downsides of hypercapnic acidosis in critically ill patients. The most widely recognized is the correlation between hypercapnia and intracranial hypertension. Hypercapnia does lead to vasodilatation, including cerebral vasodilatation. While this may augment cerebral oxygen delivery,[11] it also increases the intracerebral blood volume. If intracranial compliance is diminished, this can lead to higher intracranial pressure. This may or may not be dangerous, depending on the degree of intracranial hypertension, but it certainly bears consideration. If hypercapnia is unavoidable in a patient with significant brain injury, then intracranial pressure monitoring should be considered.

In patients with both acute and chronic pulmonary hypertension, hypercapnia can cause higher pulmonary artery pressures and lead to right ventricular dysfunction. Much of this is due to the underlying lung disease, but if there is clinical evidence of impaired hemodynamic function, then lowering the $PaCO_2$ may be beneficial.

Other systemic effects of hypercapnia are more related to the resulting acidosis than from the effect of the $PaCO_2$ itself. These include impaired cardiac contractility, prolonged QT interval, decreased systemic vascular

resistance, and hyperkalemia. If these occur, then buffer therapy may be warranted if other methods of correcting the respiratory acidosis would result in lung injury.

On a microcellular level, hypercapnia has been associated with increased tissue nitration and the production of peroxynitrite. This radical is released during conditions of physiologic stress and may mediate tissue damage.[12] The significance of this in clinical medicine is yet to be determined. Neutrophilic activity against bacterial infection is also attenuated with hypercapnia, but this can be overcome with the administration of antibiotics.[13]

Summary and Recommendations

Permissive hypercapnia is a proven strategy for reducing VILI in patients with severe respiratory failure, be it due to ARDS or obstructive diseases like asthma or COPD. To state it simply, it’s more important to prevent iatrogenic lung injury than to get “normal” gas exchange. The degree to which permissive hypercapnia has a clinical benefit beyond preventing volutrauma remains to be seen, but the existing literature suggests that this may be the case.

Chapter 7
Monitoring the Ventilated Patient

Minute-by-minute monitoring of critically ill patients is a key part of the Intensive Care Unit. As discussed earlier, the respiratory status of a patient can be evaluated with clinical examination, a chest X-ray, and an arterial blood gas. These aren't continually performed, however, and we need tools that allow us to know immediately when there is a change or deterioration in the patient's condition. Pulse oximetry is now used universally to monitor oxygenation. Waveform capnography also can provide some key information and is very helpful, but it is not used on every ventilated patient.

Pulse Oximetry

Pulse oximetry uses two wavelengths of light—red, with a wavelength of 660 nm, and infrared, with a wavelength of 940 nm. Oxygenated hemoglobin preferentially absorbs the infrared light and allows the red light to pass through the tissues; deoxygenated hemoglobin, on the other hand, absorbs red light but not infrared light. When the sensor is placed on a highly vascularized but thin bed of tissue like a fingertip, earlobe, or forehead, the ratio of light absorption can be measured.[14] This is converted to display a reading of the hemoglobin oxygen saturation (SpO_2). If the sensor is applied properly and there is adequate perfusion, it is nearly as accurate as the SaO_2 measured with an arterial blood gas analyzer.

Pulse oximetry can be inaccurate if there is hypoperfusion from shock or significant vasoconstriction, either from shock or from vasoconstricting medications like phenylephrine or epinephrine. Generally, an inaccurate SpO_2 reading due to hypoperfusion or vasoconstriction will also have a poor plethysmograph—in other words, the waveform will not be well-defined, and it will not correlate with the patient's pulse. The SpO_2 also becomes less

accurate during significant hypoxemia (SaO_2 < 80%), especially with darkly pigmented skin.

Dyshemoglobinemias can also affect the accuracy of the SpO_2. Carbon monoxide binds avidly to hemoglobin and absorbs infrared light readily, which leads to a falsely high SpO_2 (98-100%, even with significant arterial hypoxemia). Methemoglobin, on the other hand, affects both infrared and red light absorption and can alter the SpO_2 to underestimate the SaO_2 with lower levels of methemoglobinemia. At higher levels of methemoglobinemia (> 35%), on the other hand, the SpO_2 tends to read 80-85% no matter what the PaO_2 or SaO_2.

Co-oximetric blood gas analysis is the best way to diagnose dyshemoglobinemias and to see what the true PaO_2 and SaO_2 are. Massimo has developed a noninvasive pulse oximeter that uses additional light wavelengths to accurately display the fraction of oxyhemoglobin, carboxyhemoglobin, and methemoglobin.

There is one situation where the SpO_2 is more accurate than the SaO_2 (the ABG measurement). In hyperleukocytosis due to leukemia (WBC > 50K) or extreme thrombocytosis (platelet count > 1M), activated leukocytes or platelets will continue to consume oxygen in the blood gas syringe before it's placed in the analyzer, leading to falsely low PaO_2 and SaO_2 measurements. Cooling the ABG sample on ice may reduce this, but in general the SpO_2 is more accurate than the SaO_2 when the WBC or platelet count is extremely high.

Causes of Inaccurate Pulse Oximetry Measurements

Carbon Monoxide Poisoning: the SpO_2 will read high (98100%) despite significant arterial hypoxemia.

Methemoglobinemia: with significant methemoglobinemia, the SpO_2 will read 80-85% no matter what the SaO_2 or PaO_2 are.

Vasoconstriction: can lead to falsely low SpO_2 readings;

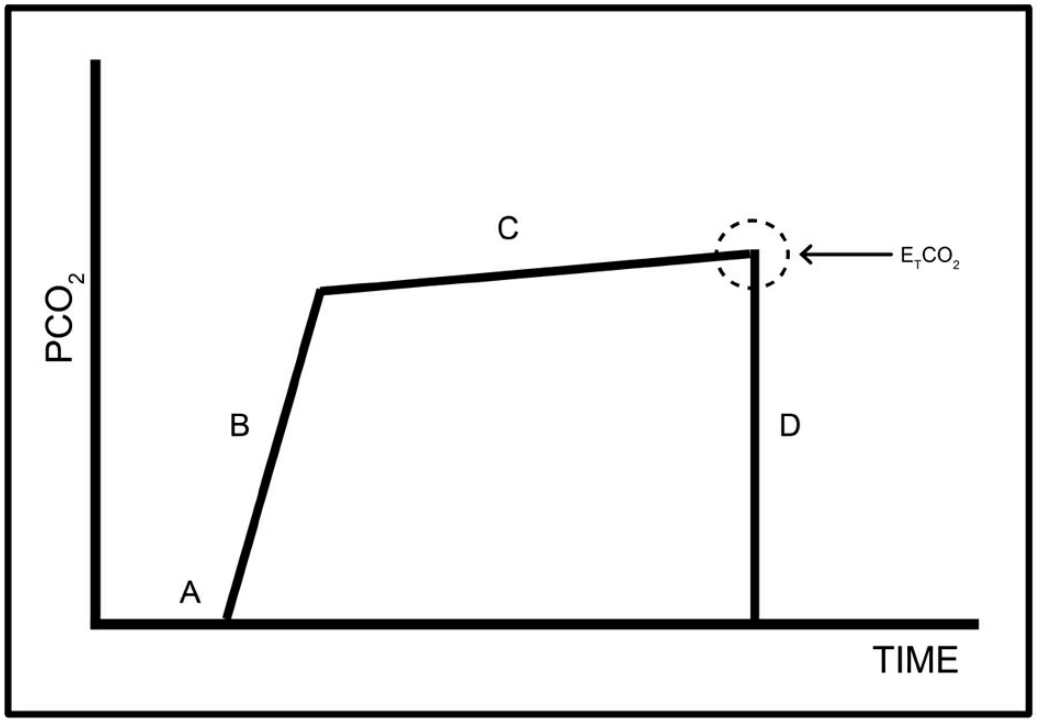
the waveform is usually poor and not correlated with the patient's pulse.

Darkly Pigmented Skin: can lead to inaccurate SpO_2 readings, but this is rarely seen except when the SpO_2 is < 80%.

Capnography

Capnometry is the measurement of exhaled carbon dioxide in numerical form, usually measured in mm Hg. Capnography is the same information, but in graphical form. In addition, the capnograph will show the pattern of ventilation. Capnography is becoming a widely accepted practice in the ICU.

Carbon dioxide is the major product of metabolism, and the exhaled CO_2 tension can be used to make assessments of the body's circulatory and ventilatory status. Most (60-70%) carbon dioxide is carried in the bloodstream in the form of bicarbonate ion— carbonic anhydrase in the RBC accounts for this. 20-30% is carried bound to proteins and hemoglobin. This leaves 5-10% to exist as dissolved carbon dioxide, which can be measured as the $PaCO_2$. This is the usual measurement of ventilation. The capnograph can provide measurement of the end-tidal CO_2 ($ETCO_2$), which, when used with the $PaCO_2$, can yield a great deal of information.



Breaking Down the Capnograph

A. Respiratory Baseline: This should be at zero. This part of the capnograph indicates the exhalation of CO_2-free air—the air in the non-ventilated parts of the tracheobronchial tree. Elevation of the baseline indicates rebreathing of exhaled CO_2. When the baseline and the $ETCO_2$ rise, this usually means the sensor is contaminated.

B. Expiratory Upstroke: This should be a steep slope, as it indicates the rapid exhalation of CO_2 from the proximal acini mixed with dead-space gas. When it is less steep, this indicates a prolongation of the time it takes for CO_2 to get from the acini to the sensor. This can be seen in cases of bronchospasm and incomplete obstruction of the endotracheal tube from secretions.

C. Expiratory Plateau: This should be horizontal, or nearly so. The end point of the plateau is the $ETCO_2$. This phase indicates the maximal ventilation of CO_2 from the lungs. An up-sloping plateau can represent incomplete alveolar emptying, such as seen in COPD, partial airway

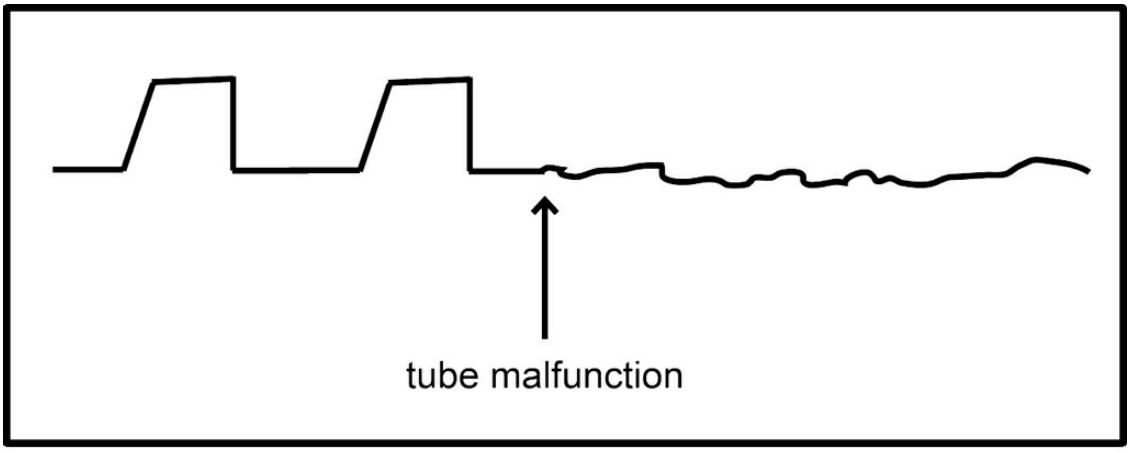
obstruction, or obstruction of the endotracheal tube.

D. Inspiratory Downstroke: The fourth phase represents the inhalation of CO_2-free gas. Leaks in the ventilator system or cuff can cause prolongation of this phase.

Clinical Use of Capnography

The first step in interpreting the capnograph should be to assess the presence or absence of a waveform. The absence of a waveform indicates one of two things:

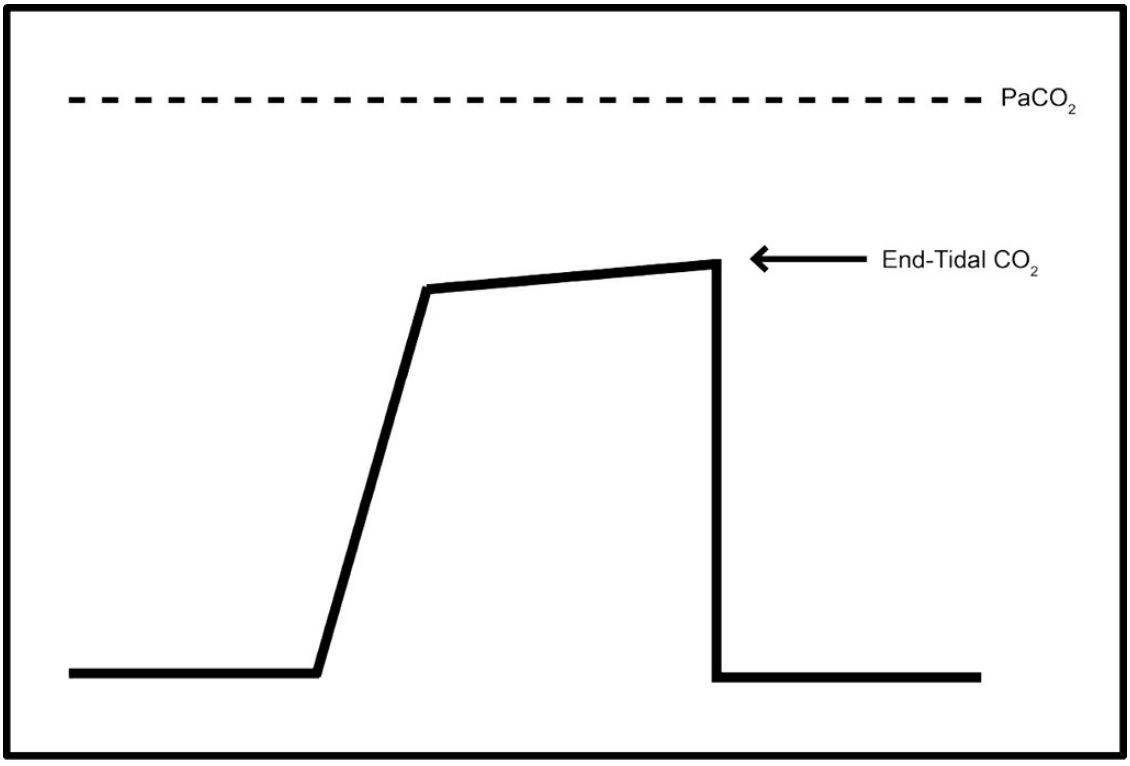
1. Failure to ventilate (esophageal intubation, dislodged endotracheal or tracheostomy tube, obstruction of the tube, apnea). THIS IS AN EMERGENCY. FIX THE PROBLEM.
2. Mechanical mishaps—fix the equipment! This should only be considered after you've thoroughly investigated #1, by the way. The CO_2 sensor can get contaminated with mucus secretions, blood, or water and may become faulty. Equipment failure is a diagnosis of exclusion once more serious causes have been ruled out.



Loss of the capnograph waveform may represent endotracheal or tracheostomy tube dislodgement; tube occlusion; or contamination of the sensor with secretions, etc. In any event, assume that the tube is not functional until that's been ruled out.

Keep in mind that the $ETCO_2$ will never exceed, and rarely match, the $PaCO_2$. The $ETCO_2$ isn't a replacement for the arterial blood gas. Knowing that the $ETCO_2$ never exceeds the $PaCO_2$ is very helpful—it means that whatever the $ETCO_2$, the $PaCO_2$ is <u>at least</u> that high. It could be a little higher, or a lot higher, but it's higher.

For example, if a patient has an $ETCO_2$ of 60, you know that the $PaCO_2$ is at least that. It could be 65, or 105, but it's at least 60. If it's important to the patient to have a $PaCO_2$ in the 35-40 range, then you know to increase the minute ventilation on the ventilator.

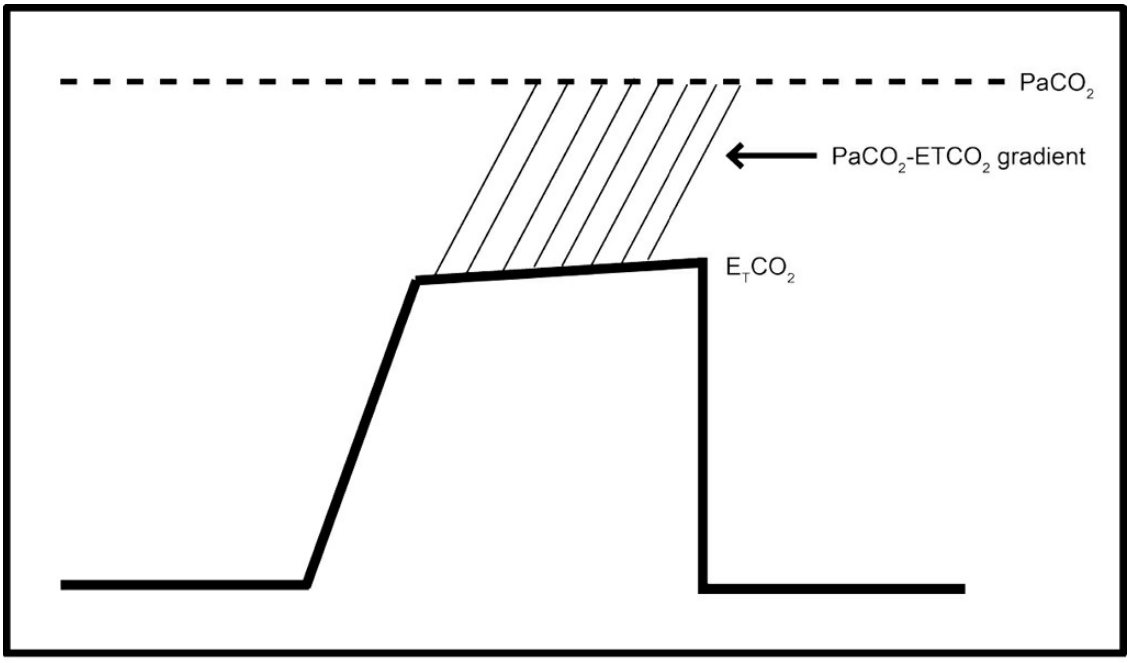


The End-Tidal CO_2 is never higher than the $PaCO_2$.

The next step is to compare the $ETCO_2$ with the $PaCO_2$. The normal arterial-alveolar CO_2 gradient is usually 3-5 mm Hg. A wide gradient means that there are areas of lung where the ventilation and perfusion aren't matched. Consider the following if there is a large difference between the $PaCO_2$ and $ETCO_2$:

- Poor cardiac function, leading to low perfusion
- Pulmonary embolism, leading to an increase in dead space
- ARDS
- VQ mismatch from COPD, pneumonitis, or other pulmonary pathology
- Hypovolemia and/or hemorrhage
- Air trapping from dynamic hyperinflation
- Overdistension of alveoli from excessive ventilator pressure

It's just as important to follow trends in the gradient. A gradient of 10 mm Hg represents a significant change in a patient who had a $PaCO_2$-$ETCO_2$ gradient of 4 mm Hg yesterday.

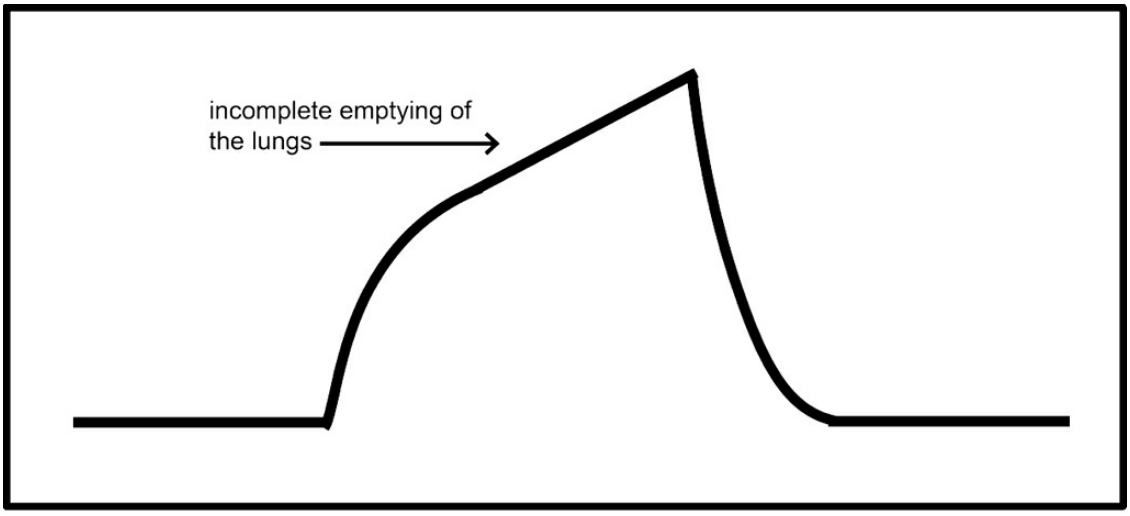


The gradient between the $PaCO_2$ and the $ETCO_2$ represents the amount of dead space ventilation. The gradient is normally < 5.

Look at the waveform and its amplitude—a discernable waveform with low amplitude usually represents a sudden increase in dead-space ventilation. However, even cardiac arrest will not drop the plateau to zero—the CO_2 in the lung must be washed out. A zero or near-zero reading, especially with an abnormal waveform, usually indicates a misplaced ETT, obstruction of the

tube, or an equipment problem. A waveform with a gradually decreasing amplitude indicates diminishing CO_2 production (hypothermia) or decreasing CO_2 delivery to the lungs (cardiac failure). A sudden increase in the $ETCO_2$ occurs when there is an abrupt increase in CO_2 production. This can occur with hyperthermia, after a seizure, bicarbonate administration, reperfusion of an ischemic limb, or ROSC after cardiac arrest.

With severe bronchospasm and other causes of increased airway resistance, there is incomplete emptying of the alveoli during exhalation. This means that the capnograph will not level off as it normally should, and instead it looks more like a shark fin. If you see this, evaluate the patient for high airway resistance.



This capnograph has the shark fin appearance seen with bronchospasm. The alveoli aren't able to fully empty, which keeps the capnograph from leveling off.

Capnography During Cardiopulmonary Resuscitation

CPR is often an unscientific, throw-the-book-at- 'em procedure. Capnography is a cheap, noninvasive, objective method for assessing the success or failure of various interventions. Cardiac arrest causes a wide gradient between the arterial and exhaled CO_2, due to lack of pulmonary blood flow. Narrowing of the gradient, as demonstrated by rising $ETCO_2$,

indicates increasing pulmonary circulation and therefore increasing cardiac output. Animal and human studies have shown the correlation between $ETCO_2$ and coronary perfusion pressure, the chief predictor of ROSC (return of spontaneous circulation). It also has been shown to correlate with cerebral blood flow.

Transient increases in the $ETCO_2$ can be seen with administration of bicarbonate and high-dose epinephrine. Return of spontaneous circulation will produce a sudden increase in $ETCO_2$, usually to 40 mm Hg or more.

One major advantage of using capnography in CPR is the ability to assess the efficacy of chest compressions. A drop in the $ETCO_2$ can be due to rescuer fatigue. $ETCO_2$ can also be used to guide the depth and frequency of chest compressions—this is objective data, and much more reliable than pulse palpation (usually retrograde venous flow). If the $ETCO_2$ is less than 10 mm Hg, the American Heart Association's ACLS Guidelines suggest trying to improve CPR quality by optimizing chest compressions. Additionally, a discernable waveform and $ETCO_2$ may reflect pseudo-electromechanical dissociation, which should be treated with vasopressors and fluid support.

Interpretation of Changes in $ETCO_2$

Rising $ETCO_2$, Rising $PaCO_2$:
Alveolar hypoventilation due to oversedation, diminished respiratory drive, or neuromuscular weakness.

Increased CO_2 production from hyperthermia, thyrotoxicosis, reperfusion, ROSC following cardiac arrest, etc.

Falling $ETCO_2$, Falling $PaCO_2$:
Alveolar hyperventilation due to pain, agitation, fever, etc.

Falling $ETCO_2$, Unchanged or Rising $PaCO_2$:
Increased pulmonary dead space due to pulmonary embolism, worsening cardiac function, bleeding, hypovolemia, or dynamic hyperinflation with autoPEEP.

Chapter 8

Safety Limits and Lung Protection

Since the advent of mechanical ventilation, there has been concern that the technology could be harmful rather than helpful. Positive pressure-related lung injury was described by Madge and Charles Macklin in 1944, which was confirmed by inflating calf and cat lungs to the point where pulmonary interstitial emphysema and pneumomediastinum occurred. They also correlated these observations with patients who were tracheotomized and given assisted breathing during surgery and made the astute observation that a transpulmonary pressure of about 25 cm H_2O was associated with lung injury. In the summary of the article, the Macklins note that "(w)omen in childbirth probably make much greater efforts than most men in their work," which contrasted with their findings that pulmonary interstitial emphysema was more common in men (but remains a true statement!).[15]

In 1970, Mead described the concept of "stress risers," where heterogenous alveoli could be exposed to different distending pressures within the same lung. This work introduced the concept of barotrauma with positive pressure mechanical ventilation, which was by then the standard treatment for acute respiratory failure.[16] Four years later, Webb and Tierney demonstrated that rats, when ventilated at high airway pressures (45 cm H_2O), rapidly became cyanotic and died of hemorrhagic pulmonary edema. They also found that application of end-expiratory pressure greatly ameliorated the damage, which they ascribed to surfactant depletion.[17] In 1988, Dreyfuss published another rat study where they bound the rats with wire and then ventilated them with different volumes. This study supported the idea of using end-expiratory pressure to reduce lung edema; additionally, using a lower tidal volume was better than a high tidal volume in the animal model, irrespective of airway pressure. This research helped lay the foundation for our understanding of lung-protective ventilation and the

mechanisms of ventilator-induced lung injury. In 1998, Tremblay and Slutsky published an editorial arguing that mechanical ventilation could, by way of inducing lung injury, lead to the release of inflammatory mediators and subsequent multisystem organ failure.[18] The "biotrauma" hypothesis added to what was understood about barotrauma and volutrauma and prompted a renewed interest in lung-protective ventilation strategies.

Enough about cats and rats—what about humans? As late as the 1990s, it was common practice in critical care medicine to use tidal volumes of 10-15 mL/kg of actual body weight to ventilate patients. While some lip service was paid to the idea of avoiding excessive distending pressures, the primary goal was to reduce atelectasis and normalize gas exchange. Textbooks warned against intubating patients with status asthmaticus, as the mortality was much higher among those who received mechanical ventilation. This was almost certainly due to the iatrogenic lung injury caused in the pursuit of normal gas exchange. Some of the same textbooks suggested prophylactic placement of chest tubes in patients with ARDS since barotrauma was seen as inevitable and a tension pneumothorax at 2 AM could be a fatal complication.

All of this changed in 2000 with the publication of the ARDSNet ARMA study,[5] which proved that ventilation with 6 mL/kg *predicted* (not actual) body weight (PBW) was superior to 12 mL/kg. The protocol, which used low* tidal volumes to minimize volutrauma and higher PEEP to prevent derecruitment, led to a 9% reduction in mortality despite the patients having worse oxygenation parameters. This was the study that brought the "open lung concept" from the lab to regular clinical practice.

Armed with the findings of the ARDS Network research group, one would expect that a new age of mechanical ventilation had begun, and that mortality from severe acute respiratory failure would drop precipitously. Alas, this has not happened. Trials attempting to determine the best way to set the end-expiratory pressure have not been enlightening—this is discussed in detail in the chapter on "PEEP, More PEEP, and Optimal PEEP." More frustrating is the evidence that despite a proven benefit, a considerable number of patients with ARDS still are ventilated with tidal volumes exceeding 8 mL/kg PBW. At the time of this writing, it has been 21 years since the publication of the ARMA trial. Given that it takes, on average, 17 years for new knowledge to be incorporated into clinical practice, we should be getting with the program!

One key takeaway from the trials on PEEP has been that the pursuit of

perfection is a fool's errand, and that a "good enough" approach is faster, easier, and paradoxically less likely to cause iatrogenic injury. An analogy could be taking kids bowling—the bumpers in the gutters keep the ball in the lane, where it bounces between them until it hits the pin. A perfect strike? Usually not. But not a gutter ball, either. One only has to read the history of clinical trials in critical care medicine to learn that attempts at optimization of physiologic parameters generally fall flat.* Why should mechanical ventilation be any different?

If we abandon the idea that we can "optimize" the vent, we do need to define some safety parameters for lung protection. Ventilator-induced lung injury (VILI) is real and is preventable to some degree. This chapter doesn't aim to discuss every possible mechanism or proposed solution for VILI, and it isn't intended to be an exhaustive examination of all of the factors contributing to VILI. Instead, the goal is to provide some understandable safety limits that are applicable to real-world practice in the ICU.

Compliance

In order to understand positive pressure ventilation, it's important to understand the concept of respiratory system compliance. Compliance can be expressed mathematically as the ratio between the change in volume and the change in pressure.

The compliance of the respiratory system depends on the individual compliance of its two components—the lungs and the chest wall. The normal compliance of each of these is around 200 mL/cm H_2O. Since it's very difficult in clinical practice to isolate the two (at least in living patients), we need to consider the two components working together in a parallel circuit. Remember that the reciprocal of the total resistance of a parallel circuit is the sum of the reciprocals of the resistance of each component.

$$1/C_{RS} = 1/C_L + 1/C_{CW}$$

Plugging in the normal compliance of the lungs and chest wall,

$$1/C_{RS} = 1/200 + 1/200 = 2/200 = 1/100$$

Therefore, the compliance of the normal respiratory system is 100 mL/cm H_2O. Application of 5 cm H_2O pressure via mask or an endotracheal tube should increase the volume of normal lungs by 500 mL. Any disease process that reduces the compliance of the lungs (pneumonia, atelectasis, pulmonary fibrosis, pulmonary edema, pneumothorax) will reduce the compliance of the respiratory system as a whole. Likewise, a reduction in the compliance of the chest wall (subcutaneous edema, circumferential burn, elevated intraabdominal pressure) will reduce respiratory system compliance.

With positive pressure ventilation, a certain amount of pressure is applied to the lungs by the ventilator to generate a volume, known as the tidal volume. The amount of pressure needed to get the tidal volume depends on the respiratory system compliance. The physician will decide which of these (pressure or volume) is the dependent variable and which is the independent variable.

If you choose to make the tidal volume the independent variable, then the mode is known as volume assist-control, or volume control. The tidal volume will be set, and the ventilator will provide as much pressure as it takes to reach the desired volume. If the compliance is poor, then it will take a higher amount of pressure. If the patient's compliance improves, then it will take less pressure to deliver the target volume.

You can also choose to set the inspiratory pressure—the change in pressure over the course of the delivered breath. Now, the tidal volume depends on the compliance and may vary as the compliance improves or worsens. This is known as pressure assist-control, or pressure control, ventilation.

Many people argue over the merits and drawbacks of volume control and pressure control ventilation. Each side has its adherents, but the fact remains that the two are linked by the compliance equation. The only difference is in what variable the physician chooses to control. So, much of this argument is ado about nothing. The ventilator can't give a tidal volume without positive pressure, and it can't deliver a driving pressure without generating a tidal volume.

Setting the Tidal Volume

For many years, physicians believed that ventilator-induced lung injury (VILI) was primarily due to excessive airway pressures. At the same time, higher tidal volumes were used to keep the $PaCO_2$ in the normal range and to prevent atelectasis. Over the last two decades, however, research has shown that the major factor behind VILI is volutrauma, or overdistension of alveoli. The landmark ARDSNET ARMA trial[19] demonstrated that by using a tidal volume of 4-6 mL/kg (compared with 12 mL/kg), mortality in patients with the acute respiratory distress syndrome (ARDS) or acute lung injury (ALI) was reduced by 9%. If you don't think this is a big deal, think again—since ARDS was first described in 1967, this was the first thing that was shown to improve survival!

Some have criticized the ARDSNET study for using too high of a tidal volume in the control group. However, this was probably closer to routine practice than you might think. Tidal volume should be based on predicted body weight (PBW), not actual body weight. If a man gains 200 pounds, his lungs don't get any bigger. PBW can be calculated if you know the patient's height and gender.

Calculating Predicted Body Weight

Men:

$$PBW\ (kg) = 0.91 \times [Height\ in\ cm - 152.4] + 50$$

Women:

$$PBW\ (kg) = 0.91 \times [Height\ in\ cm - 152.4] + 45.5$$

In general, the initial tidal volume should be set at 6-8 mL/kg PBW. If the patient has ARDS, then a tidal volume of 4-6 mL/kg is more appropriate. People with obstructive airway disease often need a slightly higher tidal volume (7-8 mL/kg) to prevent air trapping. There is some evidence that tidal volumes above 8 mL/kg may cause VILI even in people with healthy lungs, so exceeding this volume is not advisable.[20]

Tidal Volume Chart—Females

Height (ft/in)	4 mL/kg PBW	6 mL/kg PBW	8 mL/kg PBW
5’ 0	182	273	364
5’ 1	191	287	382
5’ 2	200	301	401
5’ 3	210	314	419
5’ 4	219	328	438
5’ 5	228	342	456
5’ 6	237	356	474
5’ 7	246	370	493
5’ 8	256	383	511
5’ 9	265	397	530
5’ 10	274	411	548
5’ 11	283	425	566
6’ 0	292	439	585
6’ 1	302	452	603
6’ 2	311	466	622
6’ 3	320	480	640
6’ 4	329	494	658
6’ 5	338	508	677
6’ 6	348	521	695
6’ 7	357	535	714
6’ 8	366	549	732
6’ 9	375	563	750
6’ 10	384	577	769
6’ 11	394	590	787

7’ 0	403	604	806

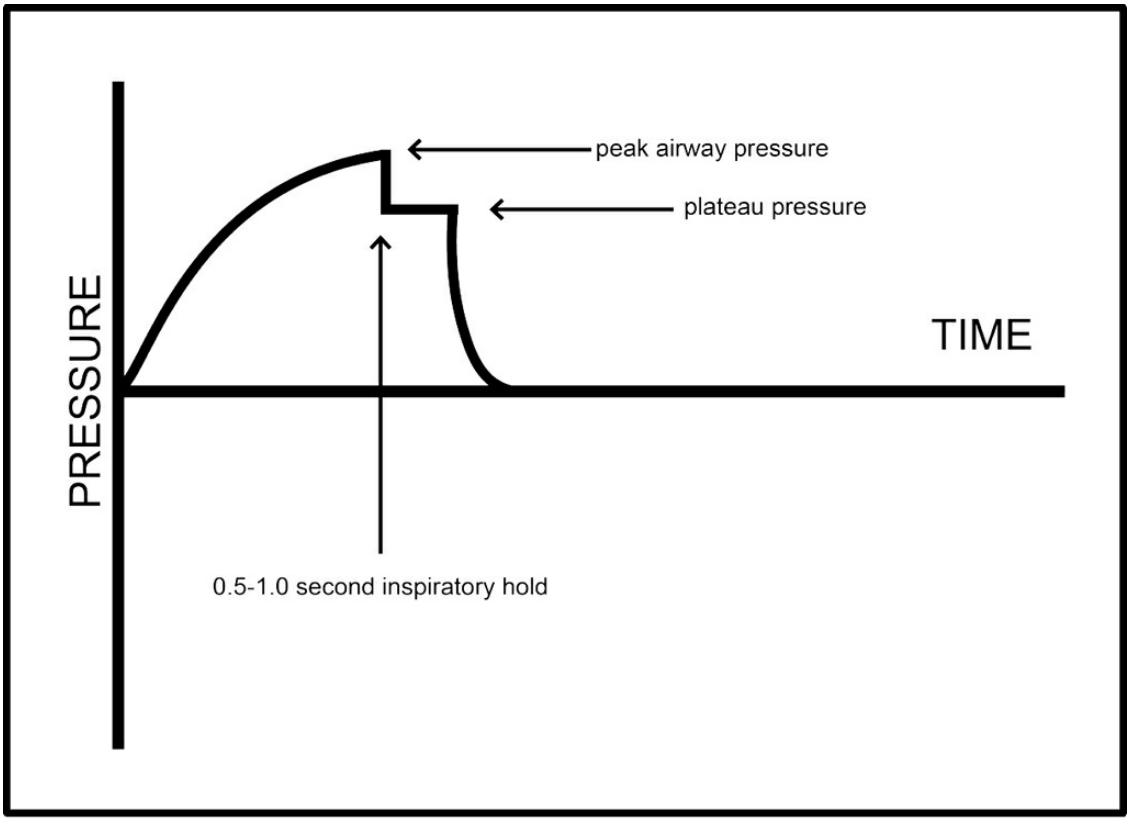
Tidal Volume Chart—Males

Height (ft/in)	4 mL/kg PBW	6 mL/kg PBW	8 mL/kg PBW
5’ 0	200	300	400
5’ 1	209	314	418
5’ 2	218	328	437
5’ 3	228	341	455
5’ 4	237	355	474
5’ 5	246	369	492
5’ 6	255	383	510
5’ 7	264	397	529
5’ 8	274	410	547
5’ 9	283	424	566
5’ 10	292	438	584
5’ 11	301	452	602
6’ 0	310	466	621
6’ 1	320	479	639
6’ 2	329	493	658
6’ 3	338	507	676
6’ 4	347	521	694
6’ 5	356	535	713
6’ 6	366	548	731
6’ 7	375	562	750
6’ 8	384	576	768
6’ 9	393	590	786
6’ 10	402	604	805

6’ 11	412	617	823
7’ 0	421	631	842

Check the Alveolar Pressure

Once the tidal volume is determined, check the distending pressure on the alveoli. This is known as the plateau pressure and can be observed by putting an end-inspiratory pause of 0.5-1 seconds on the ventilator circuit (most vents have a button designed for this purpose). When an end-inspiratory pause occurs, flow stops. You can demonstrate this on yourself by taking in a breath and then holding it for one second. At this point, pressure will equilibrate across the system, and the pressure in the endotracheal tube will equal the pressure in the alveoli.



The plateau pressure, or P_{PLAT}, represents the equilibration of pressures throughout the lungs when flow is stopped. This is the best assessment of the alveolar pressure.

The Plateau Pressure as a Safety Limit

In the ARDSNet studies, the cap on the plateau pressure was set at 30 cm H_2O. The rationale behind this is similar to the rationale for using a tidal volume of 4-6 mL/kg PBW—this is an approximation of "normal." During pulmonary function testing, breathing to total lung capacity (80 mL/kg) generates a maximum transpulmonary pressure of 30-35 cm H_2O if the lung and chest wall compliance is normal. Under normal conditions, the collagen fibers in the lung that comprise the blood-gas barrier can withstand a pressure up to 35 cm H_2O before they fracture.[21] Therefore, most lung-protective strategies prescribe limiting the P_{PLAT} to 30 and reducing the tidal volume to as low as 4 mL/kg PBW to keep the alveolar pressure at or below this

threshold.

The Problem with Tidal Volume

A review of the literature would suggest that keeping the tidal volume at 4-6 mL/kg PBW is about as close to gospel as one can get in critical care medicine. And to be fair, it's not bad. Reducing the tidal volume is associated with better outcomes, and it's an easy thing to put into a vent protocol. The problem is that a tidal volume of 6 mL/kg is taken as a one-size-fits-all setting, regardless of the severity of ARDS. A patient with mild ARDS and a PaO_2/FiO_2 ratio of 280 is given a tidal volume of 6 mL/kg. So is someone with moderate ARDS and a PaO_2/FiO_2 ratio of 120, and another person with severe ARDS who has a PaO_2/FiO_2 ratio of 75. A great deal of work has been done trying to establish the best PEEP, but relatively little prospective research has been done on the tidal volume, at least since 2000.

ARDS is a heterogenous disease, with pockets of healthy alveoli and diseased alveoli occupying the same lobes, and even segments, of the lungs. Lung-protective ventilation is designed to minimize overstretch of the healthy alveoli (volutrauma) while maintaining recruitment and preventing collapse of diseased alveoli (atelectrauma). As the lung injury worsens, fewer healthy alveoli remain to do the work of gas exchange. This is the "baby lung" concept popularized by Gattinoni—in ARDS, the lungs aren't stiff like they are with pulmonary fibrosis; rather, they are small. A full-grown man with ARDS may have the same amount of healthy lung tissue as a five-year-old child. This healthy lung tissue is what is used during mechanical ventilation and injuring the healthy tissue will only make things worse.

Consider two patients who are receiving mechanical ventilation. Patient A is a man with a PBW of 70 kg who has normal lungs and a normal chest wall. At 6 mL/kg, his tidal volume is 420 mL. The normal compliance of the respiratory system about 1 mL/cm H_2O/kg, so for this patient it's 70 mL/cm H_2O. That means that it takes 6 cm of pressure to generate the tidal volume.

Patient B also has a PBW of 70 kg, but he has ARDS. On the ventilator, it takes 21 cm pressure to generate a tidal volume of 420 mL. That means that his measured compliance is 420 mL/21 cm H_2O, or 30 mL/cm H_2O. The reduction in his respiratory compliance is often referred to as his lungs "being stiff," but that's not the issue. The healthy alveoli in his lungs have the same

compliance as Patient A's do. The difference—and this is key—is that *Patient B has a lot fewer healthy alveoli*. If healthy alveoli have a compliance of 1 mL/cm H_2O/kg, then Patient B has the lungs of a 30 kg patient. In other words, Patient B has the equivalent to the lungs of a 10-year-old child. If the ARDS gets worse, then he may be working with the lungs of a 5-year-old. As the ARDS gets better, his healthy lung volume will increase until he's finally back to having the lungs of an adult. This is the baby lung concept. The problem with using a tidal volume based on his adult size is that it ignores the amount of functional lung that he truly has.

The challenge is that it's impossible, without advanced reconstructive CT imaging, to know exactly how much healthy lung a patient has at a given time. To get an idea of the size of the baby lung, we have to consider the relationship between the tidal volume and the functional residual capacity (FRC). The FRC represents the point at end-expiration where the inward pull of the lungs is balanced by the outward recoil of the chest wall. In pulmonary function test terms, the FRC is comprised of the residual volume and the expiratory reserve volume. From a clinical medicine standpoint, think of the FRC as the lungs' reserve. The alveoli are still open at end-expiration due to the action of surfactant and the recoil of the chest wall. Because they are open, they participate in gas exchange and provide a reservoir of oxygen. Most disease states that cause respiratory failure in the ICU are restrictive, which means they reduce the FRC. This is evident when there is alveolar flooding and atelectasis on chest imaging. PEEP is used to open up collapsed alveoli and to restore some, if not all, of the FRC.

The FRC is about 35 mL/kg PBW. In our previous example, Patient A has the normal lungs of a 70 kg man. Therefore, his FRC is 2450 mL. Patient B, on the other hand, has the lungs of a 10-year-old. His "baby lung" should be based on a PBW of 30 kg, even though his actual PBW is 70 kg. His FRC is 1050 mL.

The total lung capacity (TLC) is about 80 mL/kg PBW. Exceeding TLC leads to lung injury and edema. If the TLC is 80 mL/kg, and the FRC is 35 mL/kg, then the TLC/FRC ratio is 2.3. Interestingly enough, in an animal model, exceeding a TLC/FRC ratio of 2.5-2.8 caused lethal lung injury.[22] Therefore, it seems prudent to use this as another safety limit during mechanical ventilation. Still, if we don't know the size of the baby lung (and thus the FRC), how can we stay below the limit? To answer that, we need to consider stress and strain together.

Stress and Strain

The stress applied to the lung is related to the transpulmonary pressure that the alveoli feel at the end of inspiration. Since most patients in the ICU don't have an esophageal pressure monitor, we'll stick with the plateau pressure (P_{PLAT}) and the end-expiratory pressure (PEEP) to make this calculation.* The difference between the end-inspiratory (P_{PLAT}) and end-expiratory (PEEP) pressures is called the driving pressure of the lung (P_L).

In addition to the stress on the lung, we need to consider the strain. The strain is related to the change in lung volume between the resting point and end-inspiration. The alveoli are not balloons and they don't inflate uniformly. Rather, think of the lung as unfolding during inspiration. The strain comes from conformational changes in the elastin fibers. Repetitive strain can damage these fibers and contribute to VILI.

Based on what we know already, we don't want to exceed the TLC of the healthy portion of the lungs during mechanical ventilation. The tidal volume (VT) is the end-inspiratory volume minus the end-expiratory volume. If the TLC is the maximum end-inspiratory volume we're willing to tolerated, and the FRC is the end-expiratory volume, then the VT = TLC – FRC.

If the TLC is 80 mL/kg, and the FRC is 35 mL/kg, then the maximum allowable inspiratory tidal volume is 80 – 35, or 45 mL/kg. The strain imposed on the lung during mechanical ventilation is the VT divided by the FRC. Therefore, the safety limit VT/FRC ratio is 45/35, or 1.3.

How do we reconcile the stress and strain? The answer is in the specific elastance* of the lung. Human models of both healthy and diseased lungs have shown that the specific elastance of the healthy portion of the alveoli (that is, the baby lung) is 13.5 cm H2O/L.[23] Whether it's one alveolus or a million, the specific elastance stays the same. The equation relating stress and strain is:

$$\text{Stress} = K \times \text{Strain}$$

If stress is the driving pressure (P_{PLAT} − PEEP), strain is the relationship between VT and FRC (VT/FRC), and *K* is the specific elastance of the lung, then the equation can be rewritten:

$$P_L = 13.5 \times [VT/FRC]$$

Since we've already established that the maximum safe VT/FRC ratio is 1.3, then:

$$P_L = 13.5 \times 1.3 = 17 \text{ cm } H_2O$$

By using the relationship between stress and strain, we can calculate that the maximum safe driving pressure is 17 cm H_2O. This, in effect, "indexes" the tidal volume to the FRC (which we have no way of measuring) and provides a useful way to make sure that a typical tidal volume of 6 mL/kg is still safe.

Let's go back to Patient B. He's receiving a tidal volume of 6 mL/kg, or 420 mL. He has a PEEP of 10, and a P_{PLAT} of 31. His driving pressure (P_L) is 21, which is above our safe limit. Plugging this back into our stress/strain equation, his VT/FRC ratio is 1.6. That means that the delivered tidal volume of 420 mL could be exceeding the total inspiratory capacity of the healthy alveoli.

When Patient B's tidal volume is lowered to 5 mL/kg PBW, or 350 mL, the P_{PLAT} falls to 22. His P_L is now 12, with a VT/FRC ratio of 0.9. These are both well within our safety parameters.

To date, there are no prospective clinical trials that prove that using a driving pressure-governed strategy reduces mortality. A retrospective review of the ARDSNet data, however, did show an association between a $P_L > 15$ cm H_2O and excess mortality.[24] For now, it seems prudent to consider the driving pressure when setting the tidal volume.

Stress Risers and Multipliers

If the lung were homogenously affected, then we would be done—keep the driving pressure less than 17, keep the plateau pressure less than 30, and move on. Unfortunately, ARDS and other forms of lung injury affect different lung units differently. Open alveoli are often adjacent to flooded or collapsed alveoli, and the walls of the collapsed alveoli tug on the walls of the healthy alveoli. When stress (e.g., a change in pressure) is applied, the

effect on the healthy alveoli is multiplied. Mead[16] demonstrated this by hanging a weight from different cables, and then computing the sum of stresses if one or more cables were cut. Theoretically, the stress generated on a healthy alveolus could be multiplied by up to 4.64 if it were surrounded by diseased alveoli. In other words, a plateau pressure of 30 could generate a transpulmonary pressure of 140 cm H_2O! In practice, the multiplier seems to be closer to 2.0 in humans, but the concept remains the same.[25] This is most pronounced in areas of atelectasis, which supports the idea that opening up the lungs, and keeping them open, will minimize dynamic injury.

PEEP and prone positioning can be used to mitigate the effect of stress multiplication. PEEP acts as a moderator by recruiting collapsed lung units and preventing them from collapsing at end-expiration. This, in effect, spreads out the stress among more lung tissue—to use Mead's example, it provides more cables to support the weight. This generally requires a moderate amount of PEEP (5-15 cm H_2O). Too low, and the effect won't be enough to reduce atelectrauma. Too high, and the alveoli septae can rupture, leading to hemorrhagic pulmonary edema. High PEEP also can compromise right ventricular function.

Prone positioning can also be used as a stress moderator. Much of the lung collapse in ARDS is due to gravitational compression, so it follows that periodically changing from supine to prone would help open up collapsed lung units. Prone positioning also helps "homogenize" the intrathoracic pressure among lung units. The anterior chest moves forward easily during respiration. During mechanical ventilation, this means that the ventral lung units get the bulk of the ventilation while the dorsal lung units remain collapsed. The back, on the other hand, is more constrained by the ribs, spine, and scapulae. When a patient is placed in the prone position, his chest excursion is limited by the padding and bed, and therefore the breath delivery is spread more evenly throughout the lungs.

Airway pressure release ventilation (APRV) may also help mitigate differential stress within the lungs. Remember that the lungs aren't elastic the way a rubber band or a balloon is—that is, when there's a change in airway pressure, lungs don't immediately inflate or deflate. Instead, they are viscoelastic in the way that putty or Play-Doh is. A change in pressure will inflate the lungs, but it takes more time for the alveoli to unfold into a fully inflated form. Likewise, a sudden drop in airway pressure will lead to alveolar collapse, but over time. APRV uses a prolonged high pressure, with

periodic releases, to open up and stabilize the lung. The release times are short enough to permit expiratory gas flow while not allowing lung units to collapse. This has not been studied in the way that PEEP and prone positioning have, but the theoretical benefits suggest that APRV may also be part of a lung-protective ventilator strategy in some patients.

Oxygen Toxicity

The concern for supplemental oxygen-related toxicity has existed for decades. In the 1970s, lung injury was described in critically ill patients who were receiving an $FiO^2 > 0.6$, but keep in mind that this was also the era of low or no PEEP and tidal volumes of 10-15 mL/kg. In neonates, hyperoxemia (PaO_2 > 150 mm Hg) is associated with retinal hyperplasia and blindness. Cerebral and cardiac vasoconstriction have also been described with hyperoxemia. Reactive oxygen species (ROS) are a normal part of the cellular immune response, but in the presence of hyperoxemia the concern is that the amount of ROS formation exceeds the natural antioxidant mechanisms that keep the inflammation in check. In addition to these systemic effects, high concentrations of inspired oxygen have been associated with absorption atelectasis, ciliary dysfunction, airway inflammation, and alterations of the microbiome.

Despite these concerns, oxygen supplementation is a cornerstone of resuscitation and critical care. When an intubated patient has any kind of deterioration, one of the first steps taken by nursing and respiratory therapy staff is to “give him some Os” and turn up the FiO_2 to 1.0. There’s something reassuring about an SpO_2 of 100% and something alarming when the SpO_2 falls below 90%.

Several recent trials have examined the use of supplemental oxygen in critical care. Here are some of the key results:

- Hyperoxemia (PaO_2 > 300) was associated with a higher risk of in-hospital mortality in patients with cardiac arrest and hypoxic-ischemic encephalopathy[26]
- Routine administration of 8 L/min oxygen to patients with ST-elevation myocardial infarction was associated with a larger infarct

size and a higher rate of recurrent MI[27]

- Conservative oxygen therapy, targeting a PaO_2 of 70-100 and SpO^2 94-98%, led to less mortality[*] than a liberal strategy (PaO_2 up to 150, SpO_2 97-100%)[28]
- Targeting an SpO_2 of 91-96% had no effect on mortality or length of stay when compared with a goal of 91-100%[29]

So, what are we to make of this? There are many theoretical benefits to avoiding hyperoxia, including minimizing absorption atelectasis and vasoconstriction. More importantly, there doesn't appear to be harm associated with keeping the patient normoxic. The ARDSNet studies aimed for a PaO_2 of 55-80 and an SpO^2 of 8894%. Experience with VV ECMO, and now with COVID-19, suggests that isolated hypoxemia isn't detrimental so long as the overall oxygen delivery is sufficient to meet the patient's metabolic needs. The safest practice, then, is to treat oxygen like any other drug and to only give the patient as much as he needs. A useful analogy is the administration of norepinephrine in septic shock. A normal mean arterial pressure is 93 mm Hg, but organ perfusion is adequate with a mean arterial pressure of 65 mm Hg. Norepinephrine is titrated to achieve the lower target since that's all that's necessary. Aiming for the higher, "normal" target would require higher doses of norepinephrine and expose the patient to the risk of harm (ischemic fingers and toes, splanchnic vasoconstriction, increased afterload leading to impaired cardiac function, etc.).

Keep in mind that this is different from "permissive hypoxia," which aims for a sub-normal oxygen saturation. While that may prove to be beneficial, and also has theoretical advantages, there is not enough evidence to do this routinely.

Safety Limits in Mechanical Ventilation

- Tidal Volume: 4-8 mL/kg PBW
- Plateau Pressure: 30 cm H_2O or less

- Driving Pressure (P_{PLAT} – PEEP): 10-15 cm H_2O
- SpO_2: 88-96%
- PaO_2: 55-90 mm Hg

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* Kind of a misnomer—if a normal resting tidal volume is 5-6 mL/kg predicted body weight, then we should refer to this as "normal tidal volume ventilation." It's only low when compared with historically higher-than-normal tidal volume ventilation.

* Supranormal oxygen delivery, goal-directed therapy for sepsis, optimization of cardiac filling pressures, nutritional immunomodulation…the beat goes on.

* Most of the time, measuring the esophageal pressure (as a surrogate for pleural pressure) isn't necessary. It should be considered when there is significant chest wall restriction from obesity or if the intra-abdominal pressure is elevated.

* Throwback to basic physiology—elastance (the tendency to recoil to a resting state) is the reciprocal of compliance.

* The study was stopped short due to an earthquake, however, which understandably limited enrollment.

Chapter 9
Assist-Control Ventilation

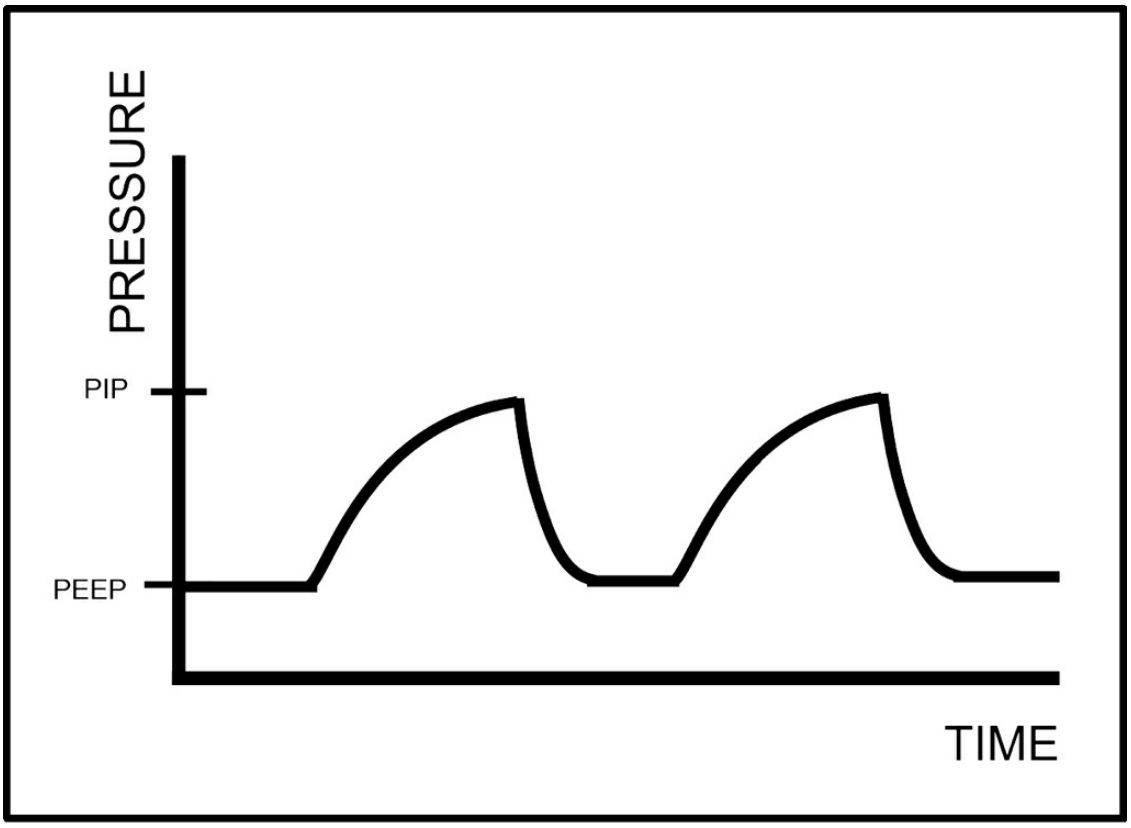
Assist-control (A/C) ventilation is the mode that requires the least effort from the patient. The ventilator will deliver a preset number of breaths per minute, no matter what—this is the "control" part. If the patient wants to breathe more frequently than the set rate, he can (the "assist" part). When he triggers the ventilator, the machine will deliver a full breath. In other words, all the patient has to do is open the demand valve to let the ventilator's computer know that he wants a breath, and the vent does the rest.

So, if the ventilator is programmed to give 12 breaths a minute, then the patient will receive 12 breaths per minute even if he makes no effort at all. If he wants to breathe over the vent, all he has to do is generate the minimum flow or pressure needed to trigger the vent. This effectively takes over the work of breathing and is very useful for situations where the patient is unable to meet his own respiratory needs—e.g., shock, acute respiratory distress syndrome (ARDS), pulmonary edema, multisystem trauma, etc.

Volume Assist-Control

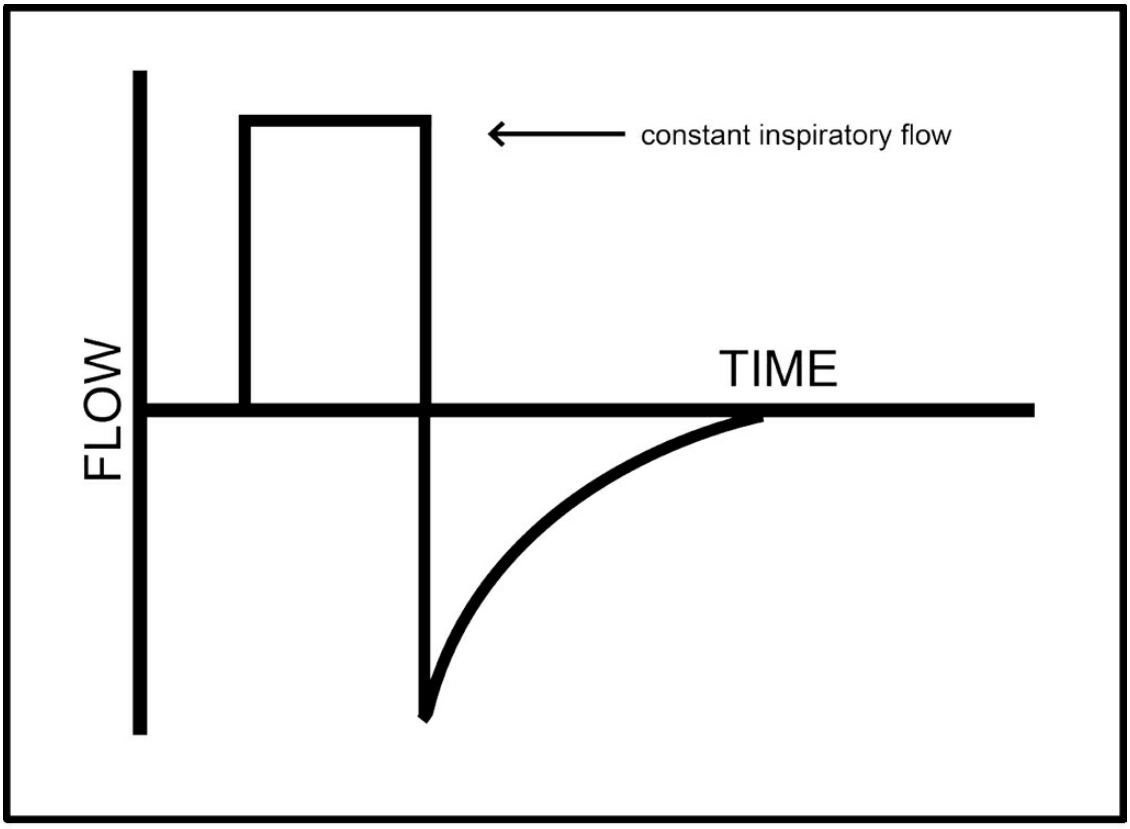
Volume assist-control ventilation (VCV) requires the physician to set a rate and a tidal volume. The product of these two numbers is known as the minute ventilation, and it is the minute ventilation that determines how much carbon dioxide is eliminated from the body. Normal minute ventilation for a healthy person at rest is between 4 and 5 liters per minute, but this can increase with fever, infection, metabolic stress, and exercise. Increasing the ventilator rate or tidal volume will increase the minute ventilation and will blow off more CO_2. Lowering the minute ventilation (by decreasing the ventilator rate or the tidal volume) will permit the arterial CO_2 tension to rise. If the patient wants to breathe over the set rate, he can. Every time he triggers

the vent, he will receive the full set tidal volume.



In volume-control ventilation, the ventilator will increase the airway pressure until the goal tidal volume is reached.

VCV delivers a constant flow of gas during inspiration until the target tidal volume is reached. The waveform on the ventilator is referred to as a “square top” inspiratory flow.



In volume-control ventilation, the ventilator will deliver a constant flow of gas until the goal tidal volume is reached, then turn off the gas. Exhalation is passive.

Patients with COPD or asthma often like this—they typically have a high degree of air hunger and getting the tidal volume in quickly helps alleviate it. Other patients, however, find constant inspiratory flow to be uncomfortable, like drinking from a fire hose. Modern ventilators may permit the clinician to select a decelerating flow instead, which usually improves patient comfort. This is discussed in more detail in the chapter on “Trigger and Flow.”

Pressure Assist-Control

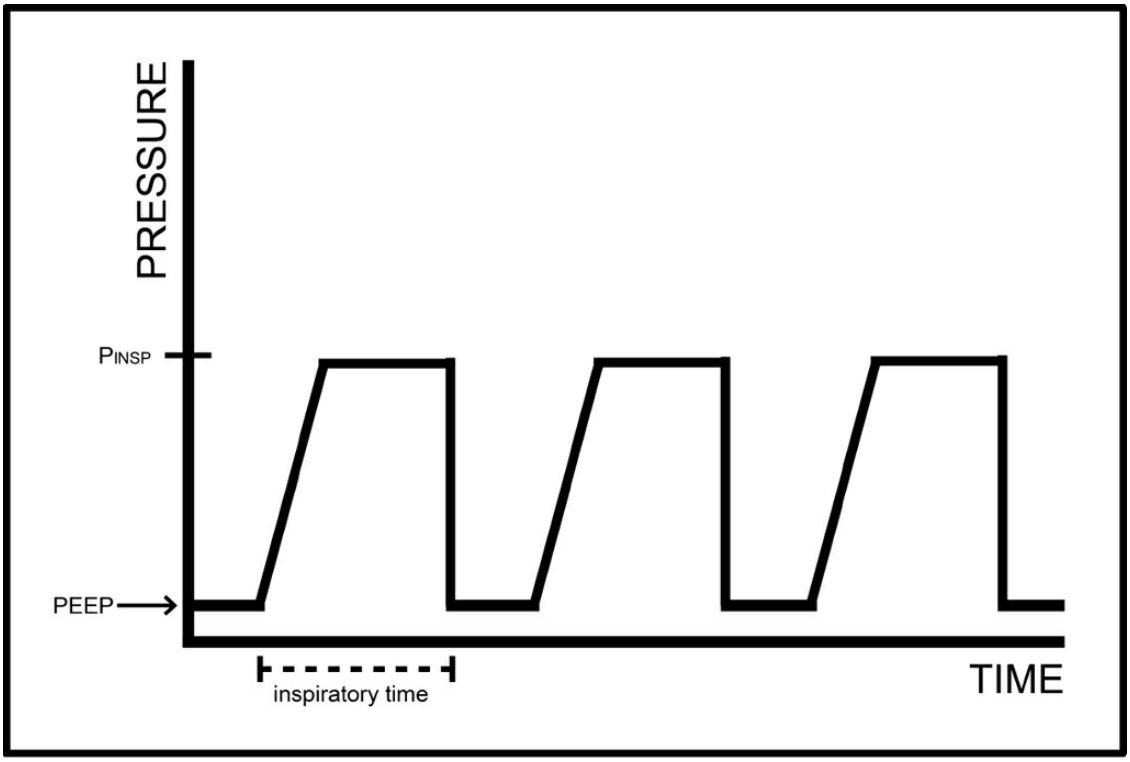
In pressure assist-control ventilation (PCV), the physician sets a rate and a driving pressure. This is the change in pressure that occurs during either a machine-administered or patient-triggered breath (remember, in assist-control the patient can breathe above the set rate). In addition, an inspiratory time (I-

time) must be selected. In VCV, the ventilator turns off the flow once the target tidal volume has been reached. In PCV, the ventilator goes up to a set pressure and will hold it as long as it's told before it turns off the flow—this is the I-time.

The ratio between the I-time and the expiratory time is known as the I:E ratio. In spontaneously breathing people, this ratio is usually between 1:2 and 1:4. In other words, breathing in takes about one second, and between two and four seconds is spent exhaling. When setting the ventilator, pay attention to the total time for each breath. If the rate is 20 breaths per minute, then it's 3 seconds per breath (60 seconds divided by 20). If the I-time is one second, then the expiratory time is two seconds—hence, a 1:2 ratio. If the rate is 15 breaths per minute and the I-time is one second, then the I:E ratio is 1:3 (60 seconds divided by 15 breaths is 4 seconds per breath).

Once the I:E ratio is 1:1 or higher, it's known as inverse-ratio ventilation. If the vent rate is 20 and the I-time is set at 2 seconds, then the I:E ratio is 2:1. Try breathing in for two seconds and then out for one—this is uncomfortable. There are special situations where inverse ratio ventilation is useful (such as severe ARDS), but it requires a great deal of sedation. In general, keep the I:E ratio between 1:2 and 1:4.

The inspiratory pressure (P_{INSP}) is the pressure change during the breath. What this means is that when it's time for a breath, the pressure rises from whatever it is at end-expiration to a peak pressure, holds for the I-time, and then goes back to the end-expiratory pressure. For example: a patient has a set rate of 15, a P_{INSP} of 20 cm, an I-time of 1.0 seconds, and a positive end-expiratory pressure (PEEP) of 10 cm. 15 times a minute, the pressure will rise from the PEEP of 10 to a peak pressure of 30 cm (Peak – PEEP = inspiratory pressure). The pressure will hold at 30 cm for one second and then return to 10 cm, the PEEP.



In pressure-control ventilation, the ventilator will go up by the inspiratory pressure and hold it for the selected inspiratory time, then terminate the breath. The tidal volume generated depends on the compliance of the respiratory system.

The tidal volume generated by the inspiratory pressure depends on the patient's respiratory system compliance. If the compliance is poor, say 15 mL/cm H_2O, then a P_{INSP} of 20 cm will yield a tidal volume of 300 mL. If the compliance improves to 30 mL/cm H_2O, then the tidal volume will also double to 600 mL. In critically ill patients, compliance can change rather quickly and result in erratic tidal volumes. Some physicians consider the lack of a reliable, guaranteed tidal volume to be a drawback of PCV. Others see this as a strength, with the rationale that tidal volumes are not usually consistent in spontaneous breathing. Whether this is a bug, or a feature, is not settled.

In general, the P_{INSP} should be set at whatever pressure generates a tidal volume of 6-8 mL/kg PBW, or 4-6 mL/kg if the patient has ARDS. As the patient's compliance improves, you will need to lower the inspiratory pressure to keep the tidal volume in this range. Even though the independent

variable is pressure and not volume, don't ignore the potential for volutrauma. The peak airway pressure (P_{INSP} + PEEP) should not exceed 30-35 cm H_2O if at all possible.

Even though the terms sound similar, it's important to distinguish the *inspiratory* pressure from the *driving* pressure. The inspiratory pressure is the pressure applied by the ventilator to generate the breath and is affected both by alveolar compliance and the airway resistance. The driving pressure is the difference between the end-inspiratory alveolar pressure and the end-expiratory pressure—in other words, the difference between the plateau pressure (P_{PLAT}) and the PEEP. Studies describing the value of measuring the driving pressure use this definition. The P_{INSP} is usually higher than the P_{PLAT} due to the additional pressure needed to overcome the resistance of the airways. The only time the P_{INSP} is the same as the P_{PLAT} is when the I-time is sufficiently long enough for the inspiratory flow to fall to zero—think of taking a breath in until your lungs are completely full and holding it. Most of the time in pressure-controlled ventilation, that doesn't occur. The I-time ends the breath before the inspiratory flow is zero, which means that the P_{INSP} is higher than the P_{PLAT}. There is a common misunderstanding that "you can't measure a plateau pressure in PCV." One only needs to do an end-inspiratory hold maneuver to see this is not the case.

An analysis of ARDS patients published in 2015 concluded that the *driving* pressure (not the P_{INSP}!) was the factor most associated with survival, even more so than the tidal volume or PEEP.[30] A threshold of 15 cm was identified as being independently related to survival, even when the plateau pressure was kept at 30 cm H_2O or less and the tidal volume was 7 mL/kg or lower. Other studies have supported this conclusion.

The inspiratory and driving pressures index the tidal volume to the compliance of the respiratory system—it's just the compliance equation written another way.

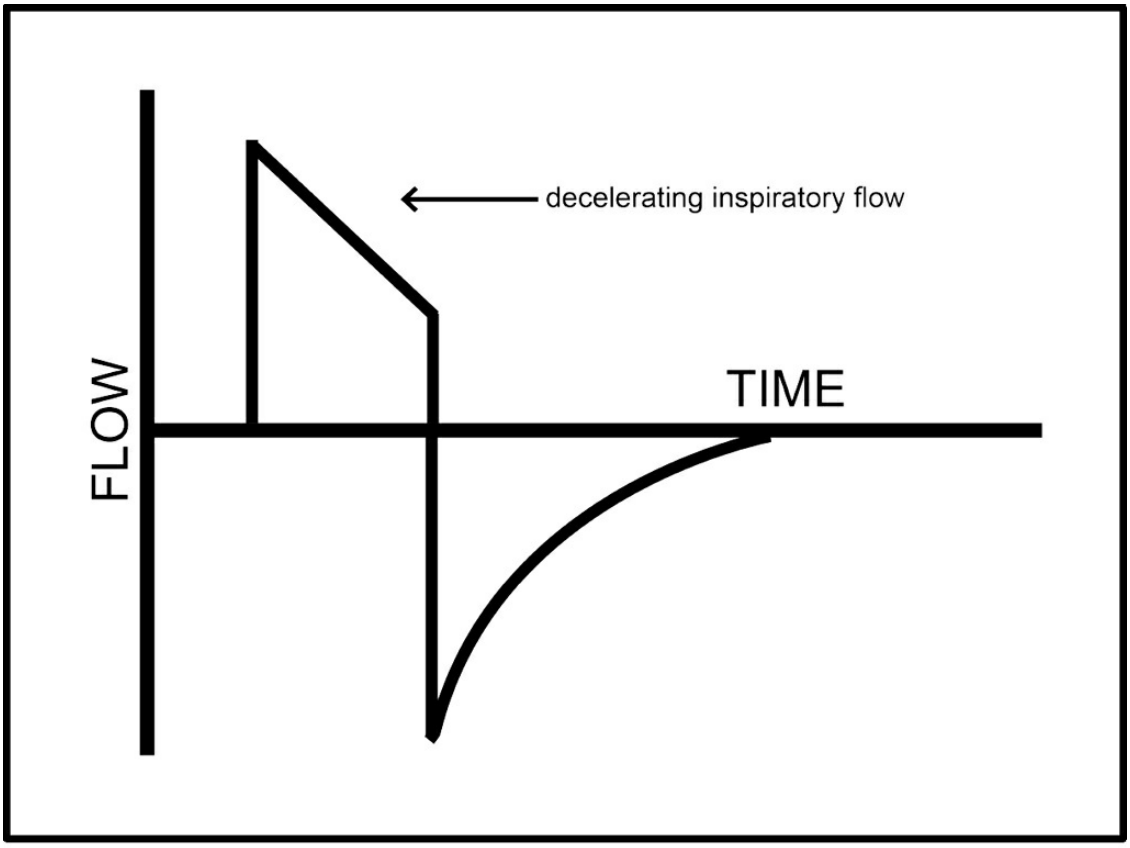
Compliance = ΔVolume / ΔPressure

C_{RS} = Tidal Volume / Driving Pressure

Driving Pressure = Tidal Volume / C_{RS}

It stands to reason that a patient with more severe ARDS will have reduced compliance, which means that it will take more pressure to get a given tidal volume. In less severe cases, the driving pressure needed to get a tidal volume of 6 mL/kg will be lower (due to better respiratory system compliance). This suggests that the driving pressure may be more of a reflection of disease severity.

PCV breaths are delivered with decelerating inspiratory flow. Because the ventilator simply goes up to the inspiratory pressure and holds it, flow of gas will naturally slow as the lungs fill. This is considered to be more comfortable than a constant, or square-top, inspiratory flow.



In pressure-control and dual-control ventilation, the flow of gas is initially high. As the lungs fill, the flow of gas slows down, or decelerates. The breath is terminated by either the end of the inspiratory time (PCV) or when the goal tidal volume is reached (PRVC and other dual-control modes). Exhalation is passive.

Dual-Control Modes

What if you could have the best of both worlds? The ability to set the tidal volume, like with volume-control, but with the comfort of decelerating inspiratory flow that pressure-control has? Have no fear—the ventilator companies have heard your requests and have developed so-called "dual control" modes of ventilation. These are known by different trademarked terms—PRVC™ (pressure-regulated volume control) by Maquet; CMV with Autoflow™ by Dräger; and VC+™ by Puritan-Bennett, to name a few. All of these do essentially the same thing, which is to deliver a volume-targeted breath with decelerating flow.

Dual-control modes ask the clinician to enter a tidal volume, a rate, and an inspiratory time. With this data, the ventilator will give the patient the tidal volume over the preset inspiratory time, adjusting the flow throughout the inspiratory cycle to get the volume in with the lowest pressure possible. The ventilator can also sense the patient's own inspiratory efforts and will adjust the flow accordingly to improve comfort.

The actual delivery of the gas is like pressure-control ventilation. In fact, if you were to look at a pressure-time and flow-time waveform for a dual-control mode, it would look the exact same as in PCV. That's because it essentially is the same thing. Imagine telling the ventilator that you want the patient to be in PCV, but the ventilator can adjust the driving pressure up or down as needed to reach a predefined tidal volume. That's what's happening here. As the patient's compliance changes, the inspiratory pressure will also change in order to keep the tidal volume where the clinician sets it. PRVC, CMV with Autoflow, and VC+ are pressure-control modes for people who don't like pressure-control.

So why haven't these dual-control modes completely replaced VCV and PCV? Most of the time, they have. Dual-control ventilation is popular because it lets the clinician control the tidal volume while delivering the volume in a more comfortable way. The peak pressures are lower than in VCV and most of the time it works very well. What's the downside?

Keep in mind that dual-control ventilation adjusts the inspiratory pressure to reach the desired tidal volume and makes changes on a breath-by-breath basis. If a patient is making spontaneous respiratory efforts, he can breathe over the vent like in all assist-control modes. If he's got a strong respiratory drive or a lot of air hunger, however, it can lead to significant patient-ventilator dyssynchrony.

Let's say that the tidal volume is set for 500 mL, and the ventilator initially has the inspiratory pressure at 20 cm. The patient pulls in a few big breaths of 800-900 mL. The ventilator's computer interprets this as an improvement in compliance—hey, the guy's getting better! —and lowers the inspiratory pressure to 10 cm. That's not enough, and the patient reacts by taking a few quick breaths of 150-200 mL. The ventilator then ramps the pressure back up, doing its best to keep the tidal volume around 500 mL. The yo-yoing pressure and tidal volume are certainly not comfortable and leads to further dyssynchrony. To the clinician, it may appear that the patient is "fighting" the ventilator and suggests the need for heavier sedation. What

actually needs to happen is for the ventilator to be changed to deliver either a set tidal volume (VCV) or a set inspiratory pressure (PCV). Dual-control modes are adaptive—that's their strength—but sometimes that adaptiveness is counterproductive.

Chapter 10

Synchronized Intermittent Mandatory Ventilation

Intermittent mandatory ventilation (IMV) was introduced in the 1970s as an alternative to assist-control ventilation. Like assist-control, the ventilator is set to deliver a predetermined number of breaths per minute. Later, the mode was improved by synchronizing the preset ventilator breaths with the patient's spontaneous breathing—if the machine detects that the patient is breathing, it will delay the machine breath to prevent a machine-given breath from occurring while the patient is exhaling. This synchronization is what puts the S in SIMV.

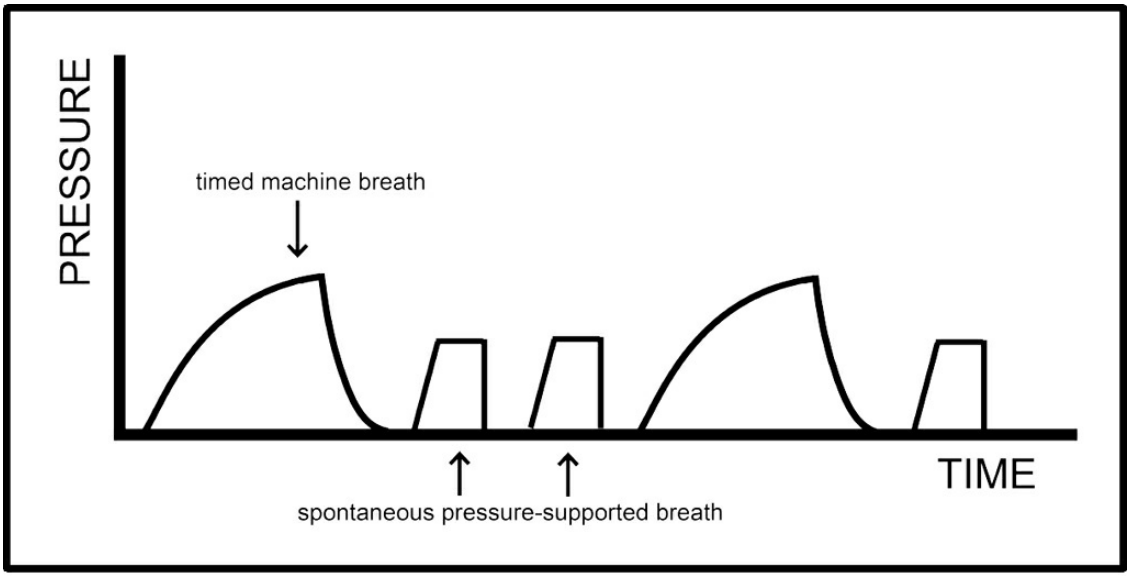
Most commonly, the machine-delivered breaths are volume-controlled (e.g., the physician sets a tidal volume). This is not the only option, though—many ventilators will allow the IMV breath to be pressure-controlled, or volume-controlled with decelerating flow. This part is no different from assist-control ventilation.

Unlike assist-control, in SIMV any spontaneous breathing by the patient does not result in a machine-delivered breath. In other words, he gets what he can get. For example, if the SIMV settings include a rate of 10 and a tidal volume of 500 mL, the patient is guaranteed to get 10 breaths of 500 mL per minute. If he breathes, say, 10 times a minute over the set rate, then he gets whatever volume of gas he can pull through the circuit. This will be variable and depends on the patient's strength, compliance, and degree of effort. The tidal volumes on SIMV may look like this (machine-delivered breaths in plain type, and spontaneous tidal volumes in bold):

500 – **254** – 500 – 500 – 500 – **399** – 500 – **526** – **122** – 500 – 500

This is all well and good if the patient is strong enough to pull adequate tidal volumes. If he's not, however, then breathing on SIMV can lead to a much higher work of breathing due to ineffective spontaneous ventilation. It is easier to breathe fast than deep, and someone with weak respiratory muscles may have a spontaneous respiratory rate of 30 but tidal volumes in the 150-180 mL range. In other words, barely more than the anatomic dead space! This wasted ventilation can rapidly lead to fatigue.

In order to get around the problem of ineffective spontaneous ventilation, modern ventilators can augment the patient's spontaneous efforts with Pressure Support (PS). PS is the pressure the ventilator applies whenever it detects the patient taking a breath on his own—it does not apply to machine-delivered breaths. This is why there's no PS in assist-control ventilation, where spontaneous efforts by the patient result in a full machine-delivered breath. The weaker the patient's effort, the more PS is needed to deliver an adequate tidal volume. The PS can therefore be adjusted based on the patient's total respiratory rate, spontaneous tidal volumes, and comfort. This is explained in more detail in the chapter about pressure support ventilation.



SIMV has a combination of machine breaths, with a set rate, and patient-triggered breaths. The patient-triggered breaths are "boosted" with pressure support as needed.

When a patient is first placed on SIMV, the rate and tidal volume should be set similarly to how you would do it for assist-control ventilation. That is, the tidal volume should be 6-8 mL/kg predicted body weight (4-6 mL/kg for ARDS), with a rate between 12 and 18 breaths per minute. The pressure support is usually set at 10 cm H_2O; if the spontaneous tidal volumes are unacceptably low (below 3-4 mL/kg), then the PS can be increased. As the patient recovers from acute respiratory failure, the ventilator rate is lowered while the PS is maintained. This means that the patient is depending more on his spontaneous ventilation and less on the machine. This continues until he's ready for extubation.

IMV, and later SIMV, was introduced as a method for weaning patients from mechanical ventilation sooner than could be done with assist-control. This has never been proven, though, and for good reason—the ventilator is a support mechanism and cannot do anything to make the patient recover from his illness or injury. In other words, the patient will come off the vent when he's ready, no matter what the mode of ventilation. Progressive loading of the respiratory muscles using pressure support and a reduction in the ventilatory rate hasn't been shown to improve outcomes, either. To date, the most effective method of weaning is the daily spontaneous breathing trial on either

a T-piece or low-level pressure support ventilation.[31]

Claims of preventing diaphragmatic atrophy are likewise unfounded—the diaphragm is a muscle that contracts throughout life and being on assist-control ventilation will not stop this. Atrophy of respiratory muscles is a problem with prolonged neuromuscular blockade, administration of corticosteroids, poor nutrition, and critical illness. **None of these can be prevented with a particular mode of ventilation.**

Despite this, there is nothing wrong with SIMV as long as you pay attention to the patient's work of breathing and comfort, and supplement his efforts as needed with pressure support and an adequate number of machine-delivered breaths. Daily spontaneous breathing trials should still be performed. It really comes down to the preference of physicians and respiratory therapists in a particular institution and what they feel comfortable using to treat patients.

Chapter 11
Pressure Support Ventilation

So, let's say that a patient has a competent drive to breathe but is not quite ready for unassisted breathing. Pressure support ventilation (PSV) allows the patient to breathe spontaneously. In fact, he has no choice—there's no set rate in PSV. Whether he breathes 4 times a minute or 40, that's what he gets.

PSV should not be used on patients who are deeply sedated or who are receiving neuromuscular blockade (which is just common sense). It's not the best mode for patients who are in shock, or who have high metabolic requirements, or who have severe lung injury or ARDS. In those cases, modes like assist-control are better. A/C is also better when the patient's breathing is, shall we say, unreliable—drug overdoses, status epilepticus, neuromuscular diseases, brainstem strokes, and high cervical spine injuries all can compromise a patient's ability to ventilate adequately.

Think of PSV as more of a "recovery mode." Once the worst of the initial illness or injury is over, and once the patient shows that he's able to maintain his own ventilation with a little help from the ventilator, consider using pressure support.

The pressure support provided by the ventilator augments the patient's effort. When the patient triggers the ventilator—when he initiates a breath and the ventilator senses it—the machine will increase the pressure in the circuit to a set level, permitting gas to flow from the ventilator into the patient's lungs. How much volume is delivered depends on the compliance of the respiratory system. Remember: compliance is the change in volume divided by the change in pressure. So, if the pressure support is set at 10 cm H_2O and a tidal volume of 400 mL is delivered, then the compliance of this patient's respiratory system is 40 mL/cm H_2O. As compliance improves (e.g., with resolution of pulmonary edema, or improvement in respiratory muscle

strength, or after drainage of a large pleural effusion), the amount of pressure necessary to generate a given tidal volume goes down. Think of pressure support as a boost that the patient needs to get an adequate tidal volume when he's breathing on his own.

If the triggering of the ventilator by the patient is what tells the machine to raise the pressure, or give the boost, then what tells it to stop? The answer is flow. When the ventilator first raises the pressure to, say, 15 cm H_2O, the flow of gas into the patient's lungs is at its maximum. As the lungs fill, the constant pressure will deliver less and less gas. If nothing told the ventilator to stop, gas would continue to flow until the pressure in the patient's lungs equaled the set level of pressure support. As you might imagine, this would be pretty uncomfortable. The solution is to flow-cycle the vent. The ventilator can be programmed to drop the pressure back down to baseline (either zero, or whatever the PEEP may be set at) when the inspiratory flow drops to a certain percentage of the initial rate. This is usually set at 25%, but it can be changed to improve patient-ventilator synchrony.

For example: a patient is receiving pressure support ventilation. The vent is set with a positive end-expiratory pressure (PEEP) of 5 cm H_2O and a pressure support (PS) of 15 cm H_2O. There is no set rate or tidal volume—remember, in PSV the patient is responsible for his own breathing. The PS is a boost that, depending on his compliance, will generate some sort of tidal volume. The flow-cycle (the signal for the ventilator to stop the PS) is 25%.

When the patient triggers the ventilator, the pressure rises from 5 (the PEEP) to 20 (PEEP + PS). At the beginning of the breath, the inspiratory flow is 40 liters per minute. The ventilator will keep the system pressurized at 20 cm H_2O, allowing gas to flow into the patient's lungs, until the inspiratory flow falls to 10 liters per minute (25% of the initial flow). At that point, the ventilator drops the pressure back down to 5 cm H_2O. The patient can exhale passively.

How much PS to provide depends on the patient. Remember, pressure support is a boost. If the patient gets tired, or if his compliance gets worse (pneumonia, pulmonary edema, etc.), he will need more PS. As he gets stronger, the PS can be dialed down. The best way to judge how much PS is necessary is to watch the patient. Another example: a woman on PSV has a set PEEP of 5 cm and a set PS of 10 cm. Her respiratory rate is in the high 30s and her tidal volume is in the low 200s. Clearly, this is not enough

support! Let's say you increase the PS up to 20 cm. Now, her respiratory rate is 8 breaths per minute. Her tidal volume is now between 800 and 900 mL. She's certainly more comfortable—almost *too* comfortable. A nice tidal volume is between 6-8 mL/kg of predicted body weight. Unless she's a 6'10" WNBA player, this is too much of a tidal volume. Lowering the PS to 14 cm leads to a respiratory rate of 16-20 and a tidal volume of 380-450 mL. Perfect. Looking at the patient is important—accessory muscle use, diaphoresis, tachycardia, and paradoxical abdominal breathing (where the chest and abdomen move dysynchronously) are all signs that the ventilator, as currently set, is not meeting her needs.

Weaning on PSV is pretty simple—as the patient gets better, she'll need less of a boost to breathe comfortably. As her strength improves, you can lower the PS (as described above). Once the level of PS needed for comfortable breathing is less than 10 cm H_2O, it's time for a spontaneous breathing trial. This is such an important topic that it has its own chapter in this book.

Volume Support Ventilation

Hopefully by now, you're convinced that PSV is a good thing. It does have some drawbacks, however. The first, and most serious, is that there is no set ventilator rate (I know I've mentioned this already, several times, but it bears repeating). A patient who keeps having apneic spells or who is hypercarbic despite a high level of PS should be switched to a more controlled mode of ventilation.

The second drawback is the unreliable tidal volumes generated by PSV. By unreliable, I don't mean that they can't be trusted. I do mean, however, that the tidal volume can vary greatly during PSV. Remember, in PSV the pressure support is fixed. The tidal volume generated depends on compliance and respiratory muscle strength. If the patient starts tiring out, or if the compliance gets worse, the tidal volume will fall (and the patient's respiratory rate will go up, as an attempt to maintain the same minute ventilation). A man may look great on morning rounds with a PEEP of 5 and a PS of 10—tidal volumes in the 500s, respiratory rate below 20, smiling around the endotracheal tube. By midafternoon, however, he may be getting tired. The ventilator still takes the pressure from 5 to 15 cm (PEEP + PS) every time he triggers the vent, but now he's pulling tidal volumes of 300 mL

and his respiratory rate is 35. Not ideal.

One solution to this problem would be to ask the respiratory therapist to stand by the ventilator all day long. When the tidal volume is higher than desired, he could reduce the PS; when the tidal volume drops below what's wanted, he could increase the PS. For example: on rounds, we decide that a decent tidal volume for our patient is 450 mL. After playing with the vent, we find that a PS of 12 cm H_2O produces a tidal volume of 450, give or take a few mL. Our trusted respiratory therapist goes to work. With hawk-like vigilance, he watches the tidal volume. It drops to 390—in a flash, he increases the PS to 15, bringing the tidal volume back to 450. But wait—now the tidal volume is 520 mL! Down comes the PS to 13. And so, on it goes, for what seems like a very long shift.

This solution would be a tremendous waste of manpower. What if, instead of having a dedicated respiratory therapist by each ventilator, we could ask the vent to do the work? That's what volume support ventilation is. You set a desired tidal volume and PEEP, and the ventilator automatically adjusts the pressure support up or down to get to the desired volume. The ventilator's computer analyzes the tidal volumes every three breaths and makes the adjustment. It is still pressure support ventilation—there's no set ventilator rate, and the breaths are flow-cycled—but now, the PS is working in the background and is variable.

Volume support ventilation (VSV) is a natural progression of PSV with newer ventilator technology. It adjusts to changes in patient compliance and respiratory effort while still permitting spontaneous breathing. It's easy to know how well the patient is doing on VSV—just look at the patient and at the peak airway pressure. Remember, the peak airway pressure is the sum of the PEEP and the delivered pressure support (so, a PEEP of 5 and a PS of 10 would lead to a peak airway pressure of 15 cm). VSV adjusts the PS up and down to get to a desired volume. So, let's say the desired volume is 450 mL and the PEEP is 5 cm. When we first put our patient on VSV, his peak airway pressure is 17 cm. This means that the PS necessary to get the volume we want is 12 cm (17 – 5). The next day, the peak airway pressure is 22 cm. This means that the patient needs more pressure—more of a boost—than he did before.

The day after that, the peak airway pressure is now 9 cm. The patient looks better, and he needs less of a boost to get his tidal volume of 450 mL. Definite improvement. In fact, since he needs a PS less than 10 cm H_2O, it's

time for a spontaneous breathing trial.

Chapter 12

CPAP, PEEP, and Optimal PEEP

In high-school science, we were taught that breathing in brings oxygen to the bloodstream and breathing out clears carbon dioxide from the body. This is true—in a bulk flow of gas sense. However, we know that gas exchange doesn't stop when you stop breathing for a few seconds, or even a few minutes. Pulmonary blood flow and alveolar gas exchange still occur, in a space called the functional residual capacity (FRC). The FRC is the "reserve zone" of the lung that maintains these vital functions even during temporary interruptions in breathing (like when you swim underwater or get a piece of meat lodged in your larynx). If we didn't have this, it would be tough to survive! If you were lying in bed and someone dropped a large heavy sandbag onto your chest, you would immediately find it difficult to breathe. This is because the weight is impairing the excursion of your respiratory muscles and compressing the FRC. On the other hand, if you were warned about the weight a few seconds before it was dropped on you, you would take a breath in and splint your chest and abdominal muscles to limit the impact. You're probably doing this right now, just thinking about the weight falling onto your chest.

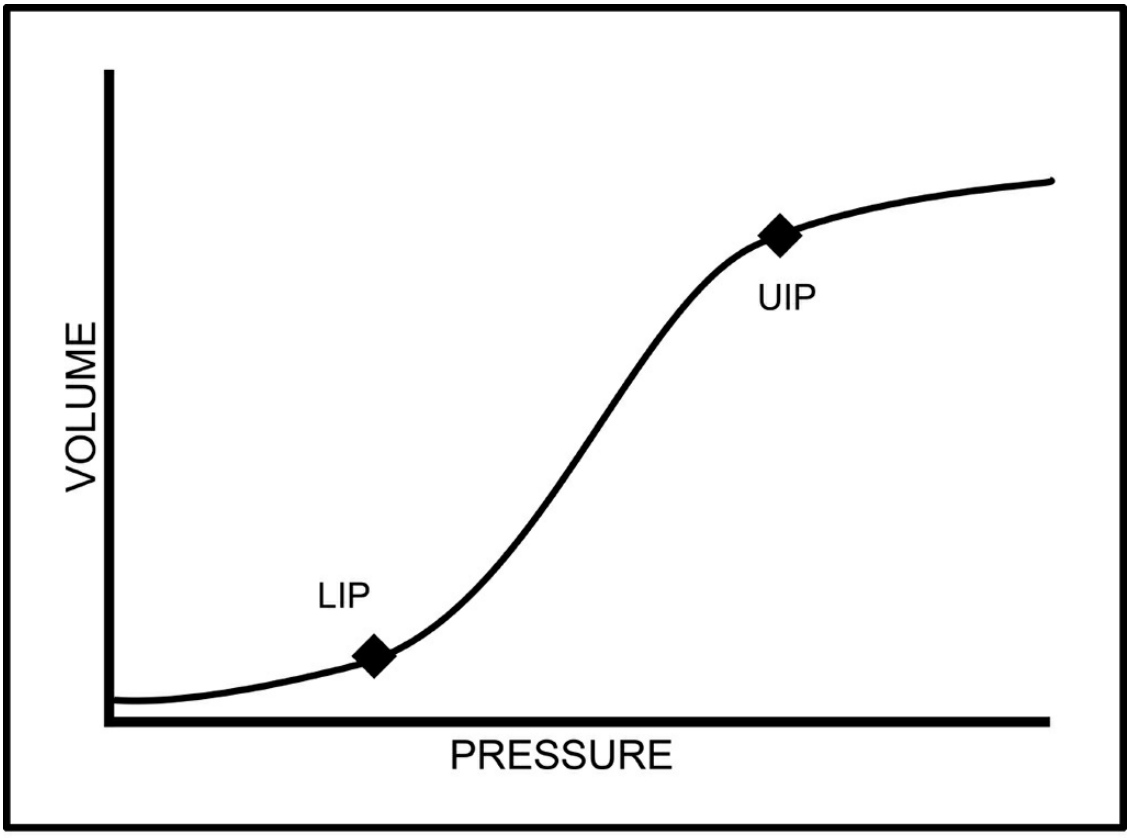
One more illustration—if you were to ride in a car and hang your head out the window at highway speeds, you would feel a rush of air into your mouth whenever you breathed in, and a resistance whenever you exhaled. This, in effect, is what continuous positive airway pressure (CPAP) is—a pressure applied to your respiratory system during both inhalation and exhalation. CPAP is applied during spontaneous respiration.

Positive end expiratory pressure (PEEP) is very similar, and is the term used for this pressure-splint applied during mechanical ventilation. It's not truly CPAP, since the inspiratory pressure from the vent is also positive, but it functions in a nearly identical manner as a way to splint open alveoli that would otherwise collapse, maintaining or augmenting the FRC. Semantically,

PEEP is the term used during A/C or SIMV, while CPAP is used for noninvasive ventilation or during pressure-support ventilation.

Diseases and conditions that reduce the FRC and flood or collapse alveoli include ARDS, pulmonary edema, pneumonia, aspiration pneumonitis, pulmonary contusions, and alveolar hemorrhage. All of these lead to hypoxemic respiratory failure by increasing the shunt fraction—lung units are perfused, but not ventilated. PEEP can be applied to open up these lung units, or prevent them from collapsing during exhalation, and to reduce the shunt fraction.

PEEP and CPAP also have a beneficial effect on left ventricular function. Increased intrathoracic pressure reduces preload by a mild degree, which can help with decompensated congestive heart failure. Importantly, PEEP and CPAP also reduce left ventricular afterload. Afterload is represented by the transmural pressure across the ventricle—in other words, the pressure inside the ventricle (systolic pressure) minus the pleural pressure. Since CPAP and PEEP increase the intrathoracic pressure, in turn increasing the pleural pressure, the difference between the two (the afterload) is reduced. This has a positive effect on left ventricular function.



In a fully deflated lung, it takes an escalating amount of pressure to "pop open" the alveoli. Once that point is reached, the lung inflates easily. This "pop open" point is known as the Lower Inflection Point (LIP) and illustrates the PEEP needed to open and stabilize flooded alveoli.

As the lung inflates, it will reach a point where it's fully expanded and where further application of pressure doesn't increase the volume. This is known as the Upper Inflection Point (UIP). The UIP marks the point where alveoli can be overdistended.

This graphical representation is a good way to understand lung compliance. In clinical practice, however, determining the LIP and UIP in a ventilated patient can be very difficult.

As a general rule, PEEP should be used to correct hypoxemia when the chest X-ray has white stuff where it should be black—in other words, use PEEP when there is radiographic airspace consolidation or infiltration.

Setting PEEP by Chest X-ray

Chest X-Ray	Initial PEEP
Clear	5 cm H_2O
Scattered Infiltrates	10 cm H_2O
Diffuse Dense Infiltrates	15 cm H_2O
Bilateral White Out	20 cm H_2O

Most of the time, when you first put a patient on mechanical ventilation the PEEP will be set between 3 and 5 cm H_2O. Theoretically, this helps prevent atelectasis in the dependent lung areas and maintains ventilation-perfusion matching. In reality, it's usually done because, well, that's how it's done! This low level of PEEP is generally not harmful.

The major complication of excessive PEEP is overdistension of alveoli leading to impairment of venous return (and hypotension) or impairment of gas exchange by compressing pulmonary capillary beds. Impairment of venous return usually doesn't happen with a PEEP less than 10-12 cm H_2O—if the blood pressure falls at this level of PEEP, the patient is usually hypovolemic, and a fluid challenge is warranted. If overdistension of alveoli is affecting gas exchange, it will be in the form of increased dead space (ventilation without perfusion)—the $PaCO_2$ will rise (along with a drop in $ETCO_2$, if you're using that) and the PaO_2 will fall.

Despite what you might hear, PEEP is not the major cause of ventilator-induced lung injury (VILI). VILI is primarily due to excessive alveolar distension during inspiration and is a consequence of *volutrauma*, not barotrauma. Excessive tidal volumes, independent of the distending pressures, can lead to alveolar damage, pulmonary interstitial emphysema, pneumothorax, and pneumomediastinum. This is the rationale behind using more physiologic tidal volumes (4-8 mL/kg) than has been done in the past.[4]

Optimizing PEEP

The majority of patients with hypoxemic respiratory failure can be managed rather easily with a PEEP in the range of 5-10 cm H_2O. In those with moderate to severe acute respiratory distress syndrome (ARDS), a more intensive regimen may be required. This is known as trying to set the "best PEEP" or "optimal PEEP"—that is, the PEEP that attains the best oxygenation and compliance while minimizing the risk of ventilator-induced lung injury. Numerous clinical approaches to the problem of finding the "optimal PEEP" for a patient have been described in the medical literature, and each method has both adherents and detractors. As you might expect, each method has its strong points and drawbacks, and no one approach is superior to the rest (otherwise everyone would use it and ignore the others). These will be discussed in turn.

ARDSNet Tables

The tables used in the ARDSNet studies have the advantage of simplicity and titratability to oxygenation, which can be measured easily with an arterial blood gas or a pulse oximeter. Two tables have been published—one that uses a high-PEEP approach, and one using lower levels of PEEP. The two methods were compared head-to-head in the ALVEOLI study,[32] which did not demonstrate improved outcomes from either approach as long as a lung-protective tidal volume of 4-6 mL/kg PBW was used. This is actually advantageous to the physician—it suggests that either table can be used, depending on the patient's condition. A patient who is morbidly obese, or who has abdominal compartment syndrome, has reduced chest wall compliance and might benefit from a higher-PEEP strategy. The extrinsic compression of the lungs, combined with the poor lung compliance due to ARDS, means that a higher expiratory pressure should be used to prevent alveolar collapse and derecruitment.

On the other hand, using a lower level of PEEP might be indicated in some cases. A patient with a bronchopleural fistula, or one with tenuous hemodynamics, or someone with one lung significantly more injured than the other, may get worse with a high-PEEP strategy. Since one table doesn't have any proven advantage over the other, the physician can pick whichever one seems to fit the patient better.

Using the ARDSNet PEEP Tables

- Go up and down the table as needed to keep the PaO_2 55-80, or the SpO_2 88-94%.
- According to the ALVEOLI study,[9] there is no proven benefit with using one table over the other, so pick according to the clinical condition—a patient with unstable hemodynamics or a pneumothorax may do better with the "Lower PEEP" approach, while a patient with significant blunt chest and abdominal wall trauma or obesity may benefit from the "Higher PEEP" strategy.
- In a randomized trial of 1010 patients, an aggressive "high PEEP" strategy coupled with recruitment maneuvers was associated with a higher 6-month mortality (65.3% vs. 59.9%).[33] These findings support using a lower PEEP strategy in the majority of patients with ARDS.

Lower PEEP Table

FiO_2	PEEP
30%	5
40%	5
40%	8
50%	8
50%	10
60%	10
70%	10
70%	12
70%	14
80%	14
90%	14
90%	16
90%	18
100%	18

100%	20
100%	22
100%	24

Higher PEEP Table

FiO_2	PEEP
30%	5
30%	8
30%	10
30%	12
30%	14
40%	14
40%	16
50%	16
50%	18
50%	20
60%	20
70%	20
80%	20
80%	22
90%	22
100%	22
100%	24

Decremental PEEP Trial

The rationale behind the decremental PEEP trial is that the patient's lungs should be recruited as fully as possible using a CPAP recruitment maneuver, followed by a stepwise gradual reduction in expiratory pressure until there is a drop-off in oxygenation, or compliance, or both. This has the advantage of

being easy to perform at the bedside; additionally, monitoring oxygenation is easily done with a pulse oximeter, and most ventilators will display static and dynamic respiratory system compliance.*

A decremental PEEP trial is performed as follows. Remember that you are going to **Recruit, Reduce,** and **Recruit.**

- Ensure the patient is adequately sedated. Neuromuscular blockade is not necessary as long as the patient isn't making a lot of spontaneous respiratory effort.
- Set the ventilator to an FiO_2 of 100%.
- Put the ventilator on CPAP 40 cm H_2O, with no pressure support. Hold at this level for 40 seconds (40 for 40). This is the recruitment maneuver.
- After the recruitment maneuver, change the ventilator mode to either Volume Control with a tidal volume of 6 mL/kg PBW, or Pressure Control with a driving pressure of 15 cm H_2O. Set the PEEP at 20 cm. Note the patient's compliance.
- Reduce the FiO_2 by 10-20% at a time every 5-10 minutes until the SpO_2 levels off at 88-94%.
- Once the FiO_2 has been reduced, begin dropping the PEEP in 2 cm increments every 5-10 minutes until the SpO_2 falls below 88%, or until there's a notable drop in compliance. Either of these would indicate alveolar derecruitment.
- Repeat the recruitment maneuver (40 for 40) and set the PEEP at 2 cm higher than the level where derecruitment occurred.

The disadvantages of a decremental PEEP trial include the time required to properly perform the trial, the need for deep sedation, and the possibility of hemodynamic or respiratory compromise during the recruitment maneuver. Clinical trials examining the decremental PEEP strategy have found that it may improve oxygenation and respiratory compliance but have not proven any benefit toward survival—in fact, a relatively large trial showed an

increase in 28-day mortality with a recruitment maneuver strategy.[33] That doesn't mean this should never be done—it simply means that it may not be reasonable to perform a decremental PEEP trial on every ventilated patient in the ICU. For those with moderate to severe ARDS, however, this can be a useful tool for finding an appropriate level of PEEP. It could also be worthwhile following a ventilator disconnection or after bronchoscopy.

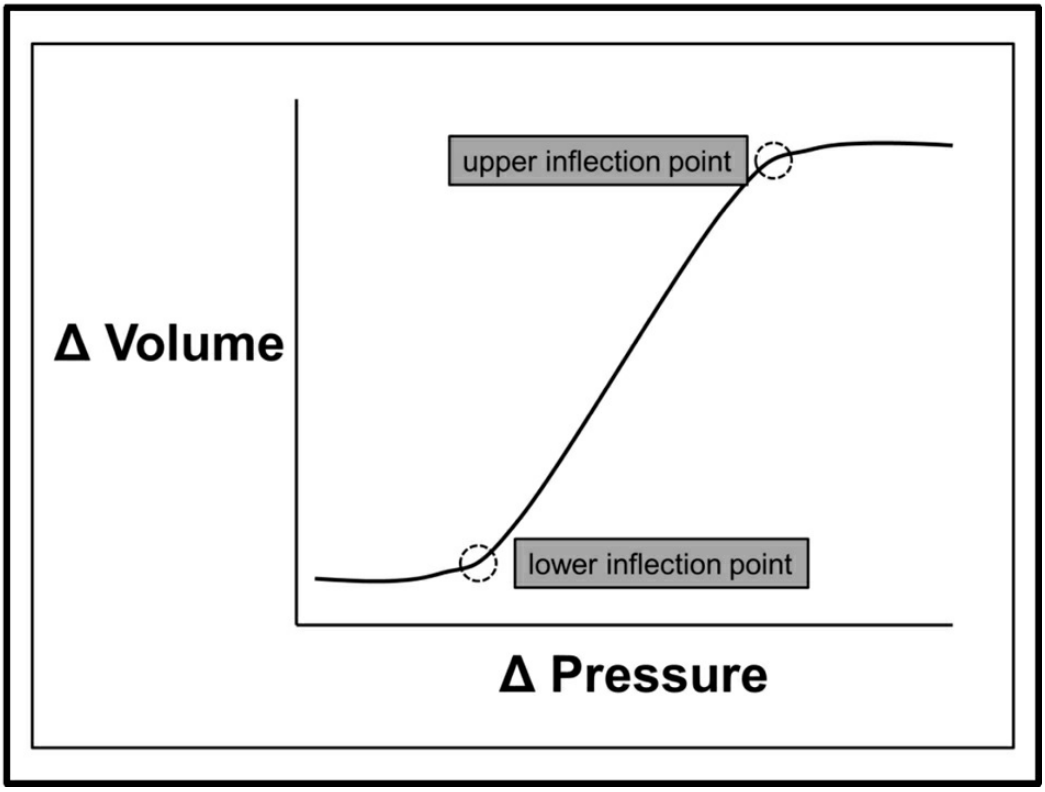
Pressure-Volume Curves

Using a dynamic pressure-volume loop to determine the optimal level of PEEP is appealing. Many ventilators can produce the P-V loop for review, and it seems intuitive that setting the PEEP at or above the point where pulmonary compliance falls would be useful.

The inspiratory limb of the P-V curve is thought to represent the change in compliance as the lungs fill with gas. Initially, the compliance (the slope of the curve) is poor, reflecting the significant inspiratory pressure needed to open collapsed lung units. Once these lung units open up, they inflate rapidly and much more easily. This is the steeper part of the inspiratory P-V curve, and it indicates that the compliance of the respiratory system has improved. The point where the compliance changes (in other words, where the slope of the curve changes) is known as the lower inflection point (LIP).

As the lungs continue to fill with gas, they reach a point where further application of pressure doesn't expand the lungs much at all—this occurs at the upper inflection point (UIP), and inspiratory pressures beyond this point are thought to contribute to alveolar overdistension and potential barotrauma.

Upper and Lower Inflection Points



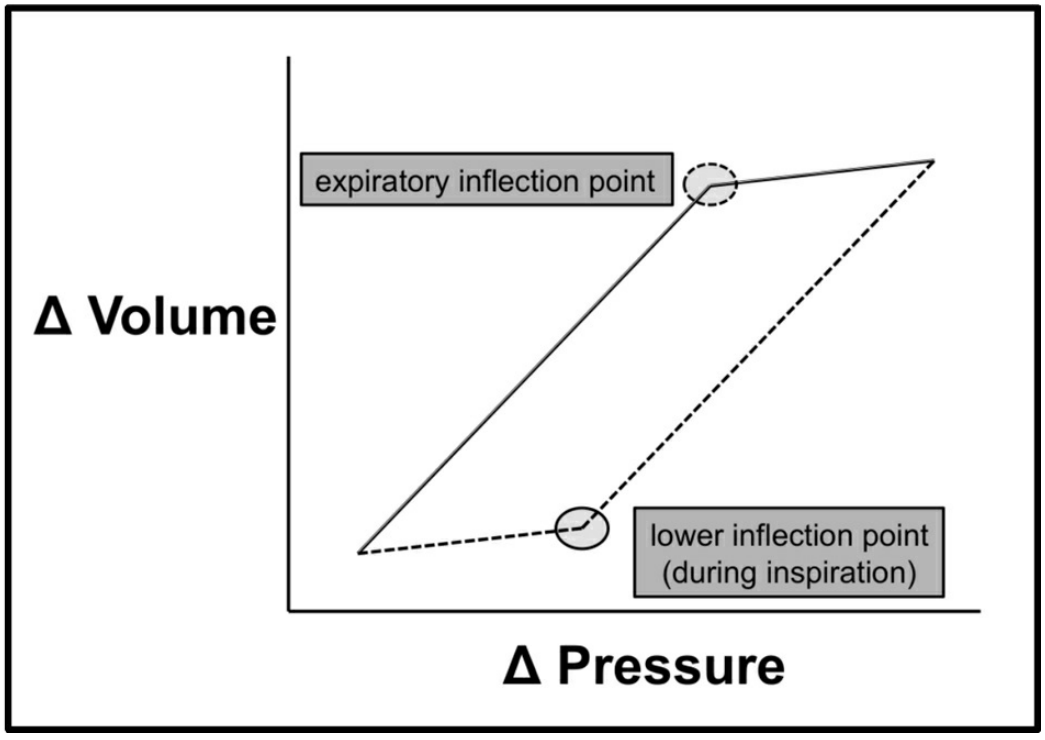
Theoretically, using the inspiratory P-V curve should tell the clinician everything he needs to know regarding the PEEP and driving pressure. The PEEP should be set at or just above the lower inflection point to keep the alveoli from collapsing during expiration, and the plateau pressure (that is, the alveolar pressure at end-inspiration) should be kept at or just below the upper inflection point to minimize overdistension and barotrauma. This would keep the patient ventilating along the steep part of the compliance curve.

Unfortunately, it's not that easy. To begin with, establishing a true pressure-volume curve is difficult. The patient can't be breathing spontaneously, because patient-initiated breathing alters intra- and extrathoracic mechanics. Neuromuscular blockade and deep sedation are often necessary. Second, the inspiratory flow must be constant and relatively low—using a decelerating inspiratory flow, which is the case in pressure control ventilation and pressure-regulated volume control ventilation, will produce an inaccurate curve. Third, the PEEP must be at zero during the maneuver, which can be risky in a severely hypoxemic patient. Fourth, and

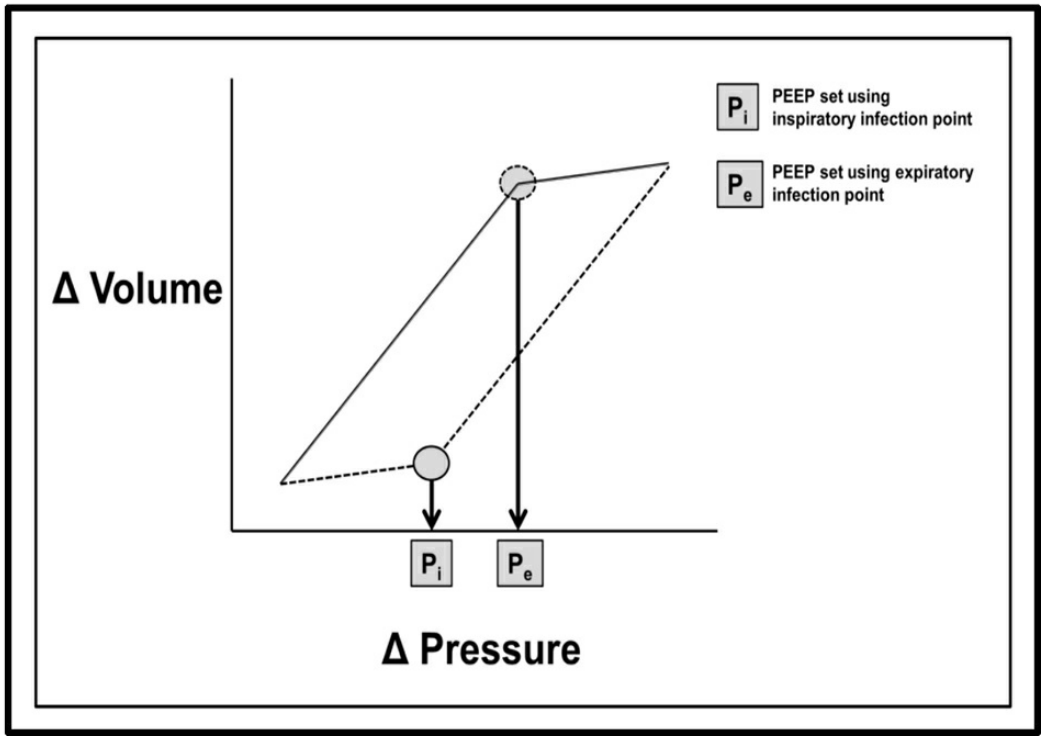
perhaps most important, is the argument that it makes little sense to set an expiratory pressure based on inspiratory pulmonary mechanics.

Clinical data in humans has shown that while there is some rationale for the lower inflection point, alveolar recruitment tends to continue during the entire inspiratory cycle. Additionally, the upper inflection point may represent the end of the recruitment process but not necessarily alveolar overdistension. During expiration, which is largely passive, an expiratory inflection point occurs at a pressure much higher than the inspiratory lower inflection point. This would suggest that alveolar derecruitment begins at a much higher pressure than the LIP, and that in ARDS this may be as high as 20-22 cm H_2O.[34] Additionally, derecruitment is affected by gravity and the position of the patient. The heterogeneous nature of both ARDS and alveolar recruitment/derecruitment makes the use of a single pressure-volume relationship difficult when it comes to setting the PEEP.

Inspiratory and Expiratory Inflection Points



PEEP At Different Inflection Points



Plateau Pressure-Guided Titration

The plateau pressure (P_{PLAT}) is the pressure measured at the end of inspiration when inspiratory flow is held at zero. This pressure reflects equilibration of pressures throughout the respiratory tree, and presumably is the end-inspiratory alveolar pressure. In general, clinicians should aim to keep the plateau pressure less than 30-35 cm H_2O, as this is felt to be the upper limit of alveolar pressure before lung injury occurs[*]. In the ExPress trial, the tidal volume was set at 6 mL/kg predicted body weight, and the PEEP was increased until the P_{PLAT} was 28-30 cm H_2O.[35] The control group had a PEEP of 5-9 cm H_2O. The hypothesis was that this would lead to full alveolar recruitment while preventing lung injury. The trial did demonstrate an improvement in oxygenation in the group receiving this intervention; however, there was no difference in survival.

One drawback of this approach is that patients with less severe ARDS may actually receive higher levels of PEEP. Take two patients with ARDS who each have a predicted body weight of 67 kg. For both, the tidal volume

should be 400 mL. If one has less severe ARDS and a respiratory system compliance of 40 mL/cm H_2O, then it will take an inspiratory driving pressure of 10 cm to deliver the tidal volume. Addition of 18 cm PEEP would bring the plateau pressure up to 28.

In the case of the second patient, assume that his condition is worse and that his respiratory compliance is 20 mL/cm H_2O. This requires a driving pressure of 20 cm to get the tidal volume, and by following this protocol, he would only get 8-10 cm PEEP to bring the P_{PLAT} up to 28-30.

This example is simplistic and purposefully ignores the fact that compliance would change (for either better or worse) with the application of PEEP, but the point is that targeting one specific number in all patients could be harmful. It is also worth considering that this method of setting PEEP did not improve survival when compared with the control group.

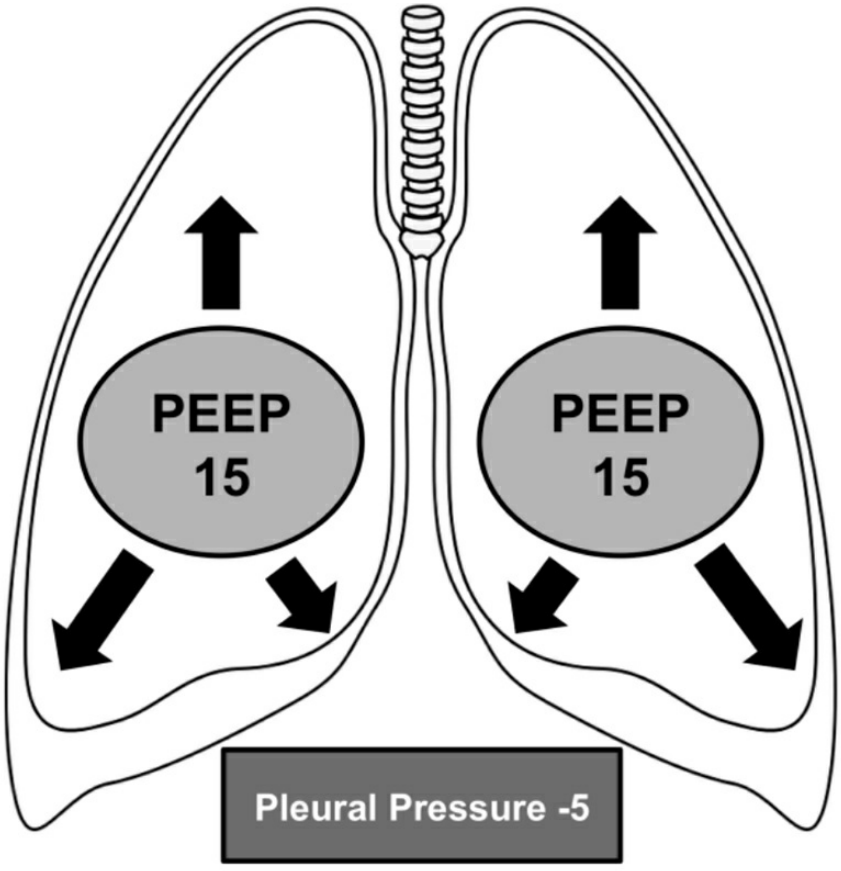
Transpulmonary Pressure

The transmural, or transpulmonary, pressure in the lung is defined as the difference between the pressure inside the alveoli and the pleural pressure. In other words, Pressure (in) – Pressure (out). Under normal conditions, this value is quite small—the alveolar pressure is atmospheric, or zero, while breathing through an open glottis, and the pleural pressure ranges from around ˍ3 cm H_2O at end-expiration to ˍ8 cm at end-inspiration. Since the transpulmonary pressure is the difference between the two, it ranges from 3 (0 - ˉ3) to 8 (0 - ˉ8) cm H^2O. This is what keeps the lungs open and acts as a counterbalance to the elastic recoil of the lung.

During positive pressure ventilation, the alveolar pressure becomes positive and ranges between the plateau pressure at end-inspiration and the end-expiratory pressure (PEEP). The pleural pressure, if unchanged, remains slightly negative. Under certain conditions, however, the pleural pressure may become positive. This usually occurs when there is a reduction in chest wall compliance either due to primary pleural disease or extrinsic compression (increased abdominal pressure, volume overload, morbid obesity, or a circumferential burn of the torso). When this occurs, the transpulmonary pressure is reduced.

Take two patients with ARDS who have a PEEP set at 15 cm. The first patient has no extrinsic chest wall restriction and a pleural pressure of -5 cm.

His transpulmonary pressure at end-expiration is 20 (15 - $^{-}$5), which serves to maintain alveolar recruitment in the setting of lung inflammation and edema.

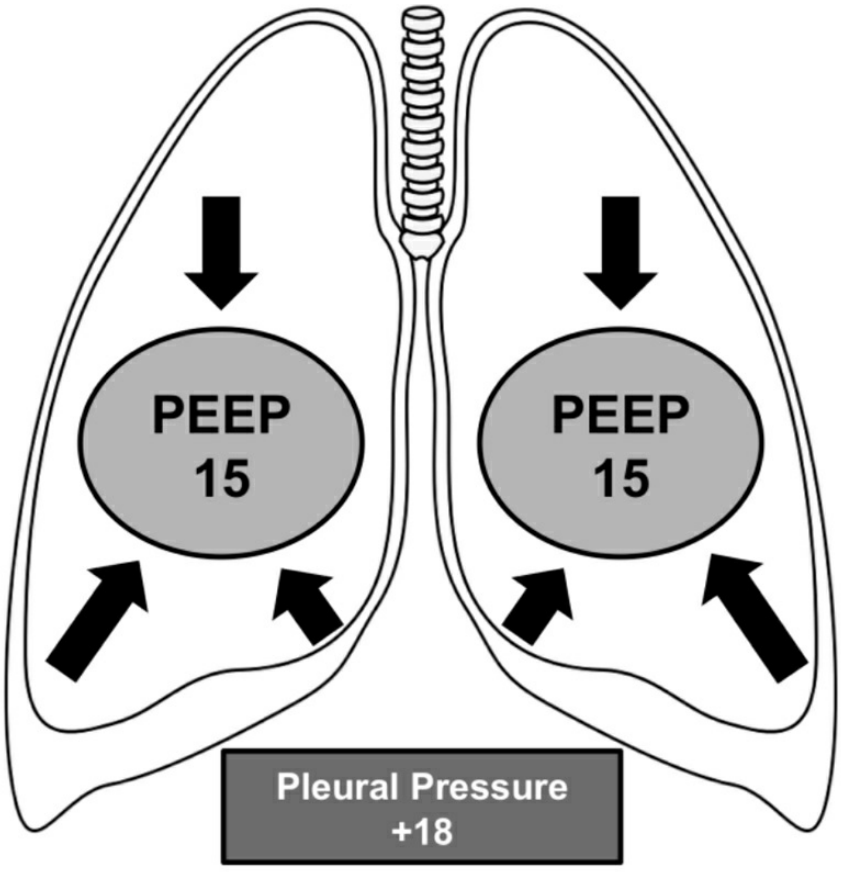


Transpulmonary Pressure = PEEP – Pleural Pressure

Transpulmonary Pressure = 15 – (-5) = 20

Net Pressure Effect Leads To Alveolar Expansion

The second patient, in addition to having ARDS, also has reduced chest wall compliance due to morbid obesity (BMI 52). His pleural pressure is +18 cm, which means that his transpulmonary pressure at end-expiration is -3 (15 - $^{+}$18). The net effect is alveolar collapse at the end of each respiratory cycle.



Transpulmonary Pressure = PEEP – Pleural Pressure

Transpulmonary Pressure = 15 – 18 = -3

Net Pressure Effect Leads To Alveolar Collapse

Direct measurement of the intrapleural pressure in ICU patients isn't possible, so the esophageal pressure is used as a surrogate. This is by no means exact—pleural pressure itself varies from the base of the lung to the apex and is affected by supine or prone positioning, and esophageal pressure is subjected to the weight of the mediastinal contents.[36] It is, however, useful for titrating PEEP in patients in whom there is considerable extrinsic reduction of chest compliance.

In order to measure esophageal pressure (P_{ESO}), an air-filled esophageal balloon catheter must be inserted. These are commercially available[37] and can be connected to a standard pressure monitoring system. The CareFusion

Avea® ventilator has a port to connect an esophageal pressure probe and can display the esophageal pressure as well.

Insertion of the esophageal balloon catheter should be done by a qualified practitioner in accordance with the manufacturer's instructions. The depth to which the catheter should be inserted can be estimated by multiplying the patient's height in centimeters by 0.288. This should, in most people, position the balloon in the lower third of the esophagus. Partial inflation of the balloon with 1 mL of air will allow changes in the esophageal pressure to be reflected on the monitor. The esophageal pressure waveform should slightly increase during ventilator-delivered breaths and have a negative deflection during patient-initiated breaths. Gentle pressure applied to the abdomen that leads to an increase in the pressure reading suggests gastric placement of the balloon, and it should be withdrawn.

Once the esophageal balloon catheter is in proper position, the end-expiratory transpulmonary pressure can be calculated:

$$\textbf{Transpulmonary Pressure} = \textbf{PEEP} - \textbf{P}_{\textbf{ESO}}$$

For a patient with a PEEP of 15 cm and a P_{ESO} of 22, his end-expiratory transpulmonary pressure is -2 cm H_2O. In other words, at end expiration the compression of his lungs by the increased pleural pressure is leading to alveolar collapse. In this situation, the PEEP should be increased to a minimum level of 17 to keep the end-expiratory transpulmonary pressure at zero.

Clinical trials examining the effect of transpulmonary pressure monitoring in patients with ARDS have demonstrated a significant improvement in oxygenation but did not show a survival benefit.[38,39] As such, this technique is not recommended for routine use. It may be helpful, though, in determining the appropriate level of PEEP for patients with intra-abdominal hypertension or morbid obesity.

Optimal PEEP vs. Good Enough PEEP

In a trial of 51 patients with ARDS, Chiumello and colleagues examined different methods of setting PEEP (ARDSNet tables, targeting a plateau pressure a la the ExPress trial, using the time-pressure stress index, and via

transpulmonary pressure using esophageal pressure measurement).[40] All methods were assessed using CT scanning to determine the change in recruitability of the lung. Their findings suggested that the only method that correlated with the degree of whole-lung recruitability and the severity of ARDS was the use of the PEEP-FiO_2 table. The other methods were associated with more hyperexpansion of normal lung units without a commensurate benefit in recruitment of collapsed alveoli.

The multiple methods of determining the best, or optimal, level of PEEP have a few things in common. They tend to be laborious. They tend to make significant physiologic assumptions that may not be valid—for example, the assumption that the pressure in the lower esophagus accurately reflects pleural pressure throughout the patient, or the assumption that lung recruitment is complete by the lower inflection point of the inspiratory pressure-volume curve. Lastly, they most often focus on surrogate endpoints that may not be meaningful. Clinical trials of different maneuvers designed to find optimal PEEP often report improved oxygenation or compliance when compared with controls, but none have shown a survival benefit.

Perhaps we need to stop searching for optimal PEEP. The history of critical care medicine has consistently shown that attempts by clinicians to optimize different physiologic parameters are often unnecessary and occasionally harmful. This may be no different. Luciano Gattinoni, one of the foremost researchers in the field, has suggested this very thing. A “good enough” PEEP maintains oxygenation and lung recruitment without compromising hemodynamic function and can be based on a combination of the severity of ARDS and the good sense of the treating clinician.

Good Enough PEEP [41]

Degree of ARDS	**PaO_2/FiO_2 Ratio**	**PEEP**
Mild	201-300	5-10 cm H_2O
Moderate	101-200	10-15 cm H_2O
Severe	≤ 100	15-20 cm

H_2O

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* Compliance = ΔVolume / ΔPressure

Dynamic compliance on the ventilator =
Tidal Volume / [Peak Inspiratory Pressure – PEEP]

Static compliance on the ventilator =
Tidal Volume / [Plateau Pressure – PEEP]

* It is important to keep in mind that no one has established a truly “safe” level of plateau pressure, above which lung injury is present and below which no injury occurs. Most experts, however, advise keeping the plateau pressure at or below this range.

Chapter 13
Trigger and Flow

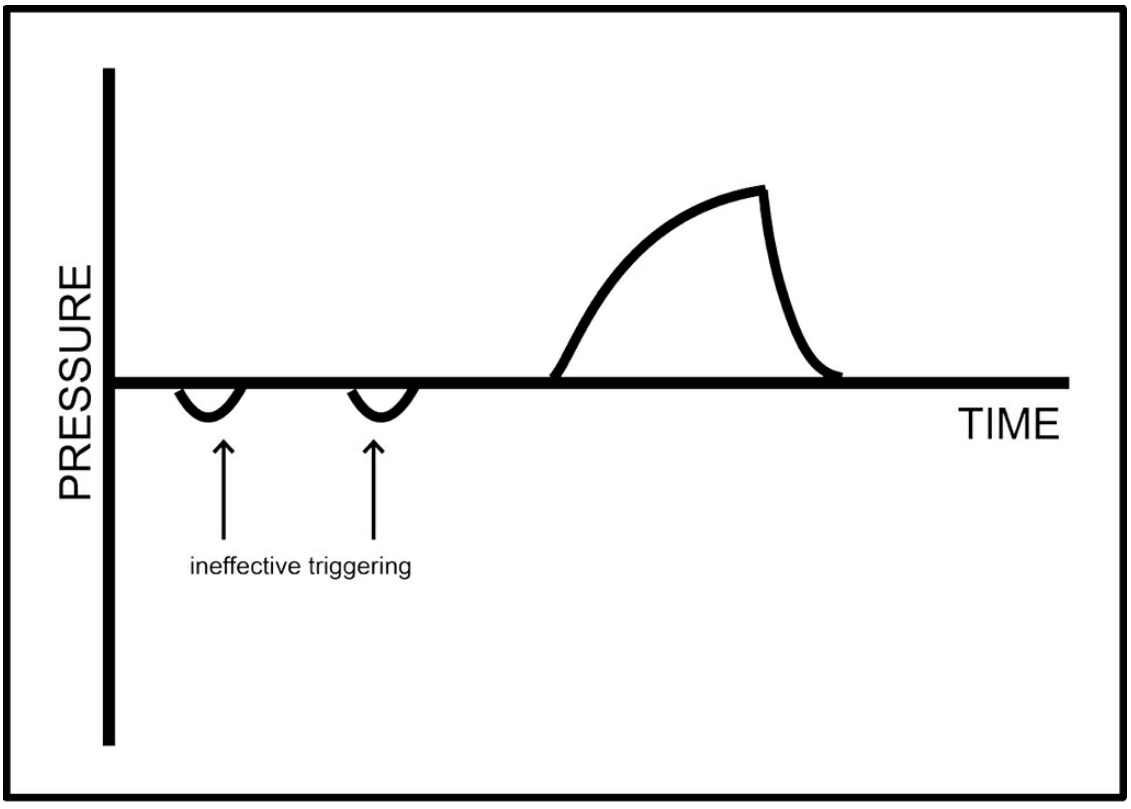
Triggering

Triggering is the term used to describe how a patient lets the ventilator know that he wants a breath. There are two types of triggering mechanisms—those that detect a change in pressure, and those that detect a change in flow.

Pressure triggering requires the patient to drop the end expiratory pressure by a preset amount—usually in the 1 to 4 cm H_2O range. This normally doesn't require a lot of effort. If the PEEP is set at 5 cm and the trigger is 2 cm, then the patient has to lower the pressure in the endotracheal tube to 3 cm H_2O in order for the ventilator to recognize that he wants a breath and to deliver it. Pressure triggering can be problematic in patients with chronic obstructive pulmonary disease, asthma, or other conditions that predispose to dynamic hyperinflation (auto-PEEP). As an example, let's say that our patient has a set PEEP of 5 but has an intrinsic, or auto, PEEP of 12. In order for the patient to trigger a breath with a 2 cm trigger, he has to get the end-expiratory pressure down to 3 cm (5 – 2 = 3). With an intrinsic PEEP of 12 cm, this requires him to generate a negative pleural pressure of 9 cm to trigger the vent. This is pretty difficult, to say the least.

Ineffective triggering can be recognized on physical exam by watching for inspiratory efforts that don't lead to a machine-delivered breath. I place my hand on the patient's chest—if I feel him trying to breathe and the vent doesn't cycle, or if there's a noticeable delay between his effort and the delivered vent, then triggering is ineffective. This can also be seen with an esophageal pressure probe, which reflects changes in pleural pressure. Negative deflections on the probe that don't correlate with ventilator cycling tell you that the patient is unable to trigger the ventilator. Physical examination is easier than placing an esophageal probe and is about as

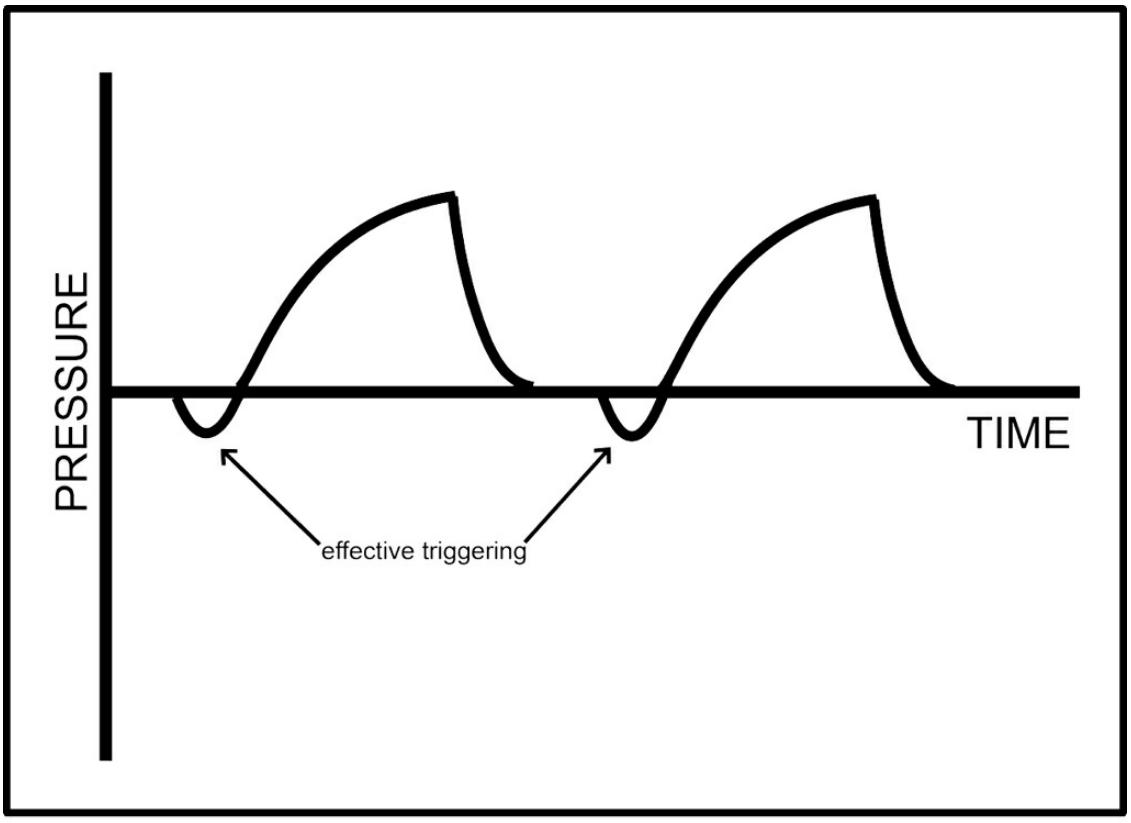
reliable.



This shows the ventilator not recognizing patient efforts to trigger a breath. This can be due to hyperinflation, respiratory muscle weakness, or if the trigger sensitivity is too low.

In order to make triggering easier, most ventilators will also allow the trigger to be initiated by changes in inspiratory flow. The trigger is usually in the range of 1 to 6 liters per minute and is independent of the patient's intrinsic PEEP. With flow triggering, the potential problem is the opposite of that seen with pressure triggering. If the flow trigger is too low, then it may "auto-cycle" the ventilator even when the patient isn't trying to get a breath. Oscillations in the ventilator tubing from water or secretions, hyperdynamic cardiac contractions, and patient movement may all be picked up by the ventilator as a change in flow and lead to a breath being delivered. On the ventilator's screen, multiple breaths stacked together indicate that this is happening. The solution is to make the trigger less sensitive, or switch to

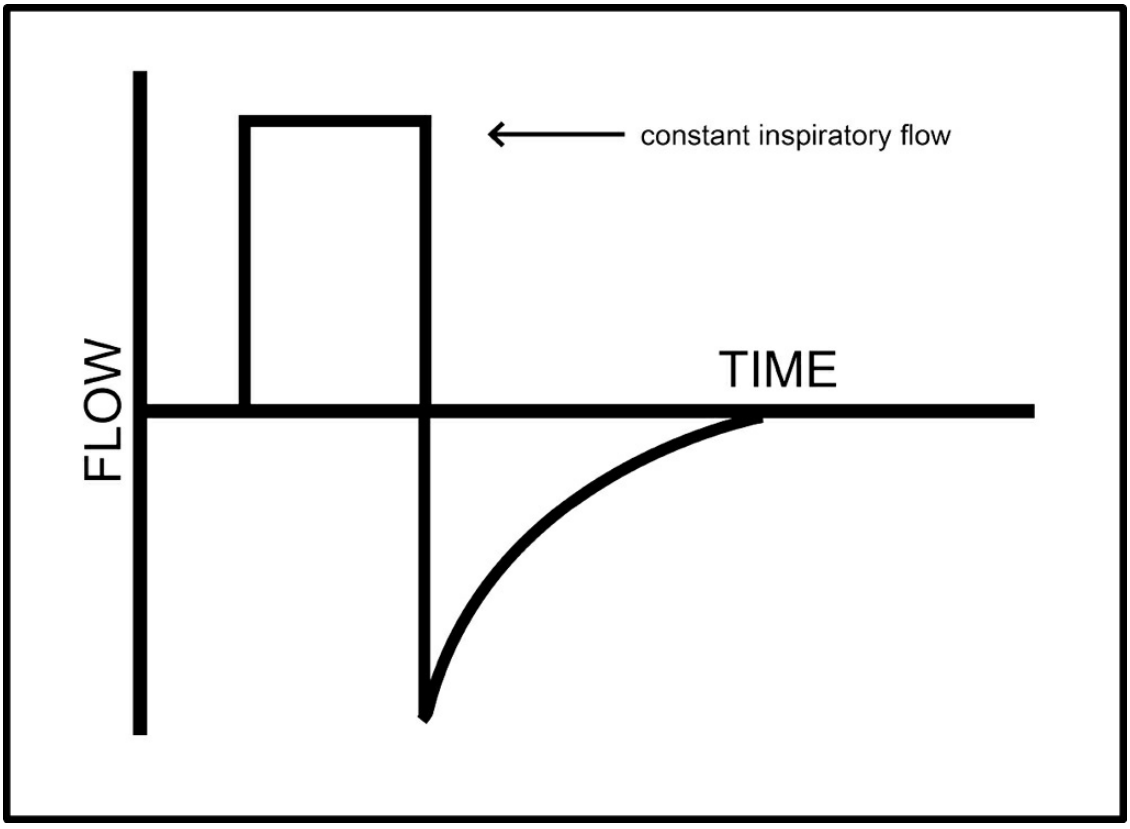
pressure triggering.



Effective triggering leads to a ventilator-delivered breath immediately following the patient's effort to breathe.

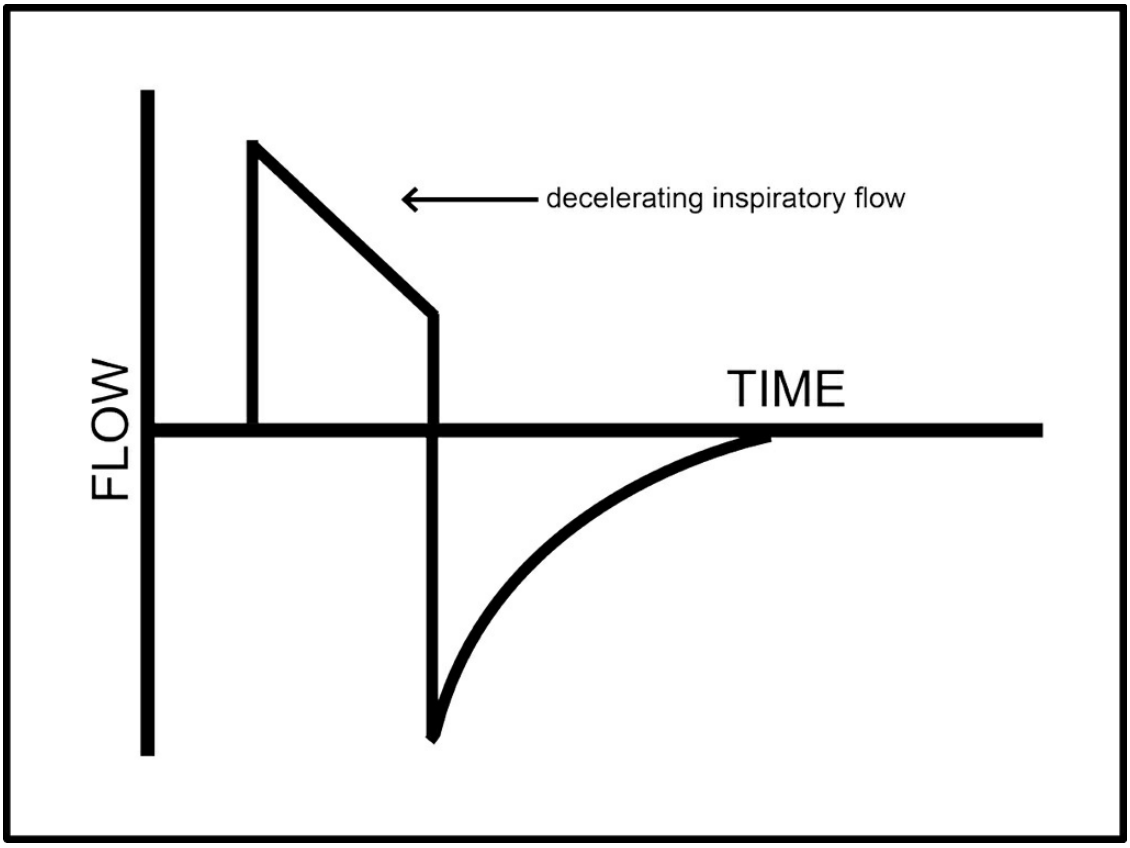
Flow

When you and I breathe, the inspiratory flow pattern is sinusoidal. Flow rapidly increases until the lungs are nearly at the tidal volume, and then it decelerates until the inspiratory flow is zero. Exhalation then occurs passively. When positive pressure ventilation is being used, the flow pattern is either constant or decelerating.



Constant flow is the pattern seen in older ventilators using volume control. When the ventilator gives a breath, it opens the valve and delivers gas at a constant rate until the target volume is reached, then shuts off the gas. This would be similar to using a compressed air hose to fill a balloon—the air will enter the balloon at a constant rate until you let go of the trigger. This appears to be a square-topped waveform on the ventilator. Constant flow is perceived by many patients to be uncomfortable—after all, it's like drinking from a fire hose. It also leads to higher peak airway pressures (but not higher plateau pressures—the pressure difference is transmitted to the endotracheal tube and the conducting airways).

Decelerating flow is the pattern seen during pressure control ventilation, pressure support ventilation, and pressure-regulated volume control; newer ventilators will also let you select this flow pattern for volume control ventilation. With decelerating flow, the waveform looks like a sloping roof. When the breath first starts, the flow is at its peak. As the lungs fill with air, the inspiratory pressure stays constant, and the flow decelerates.

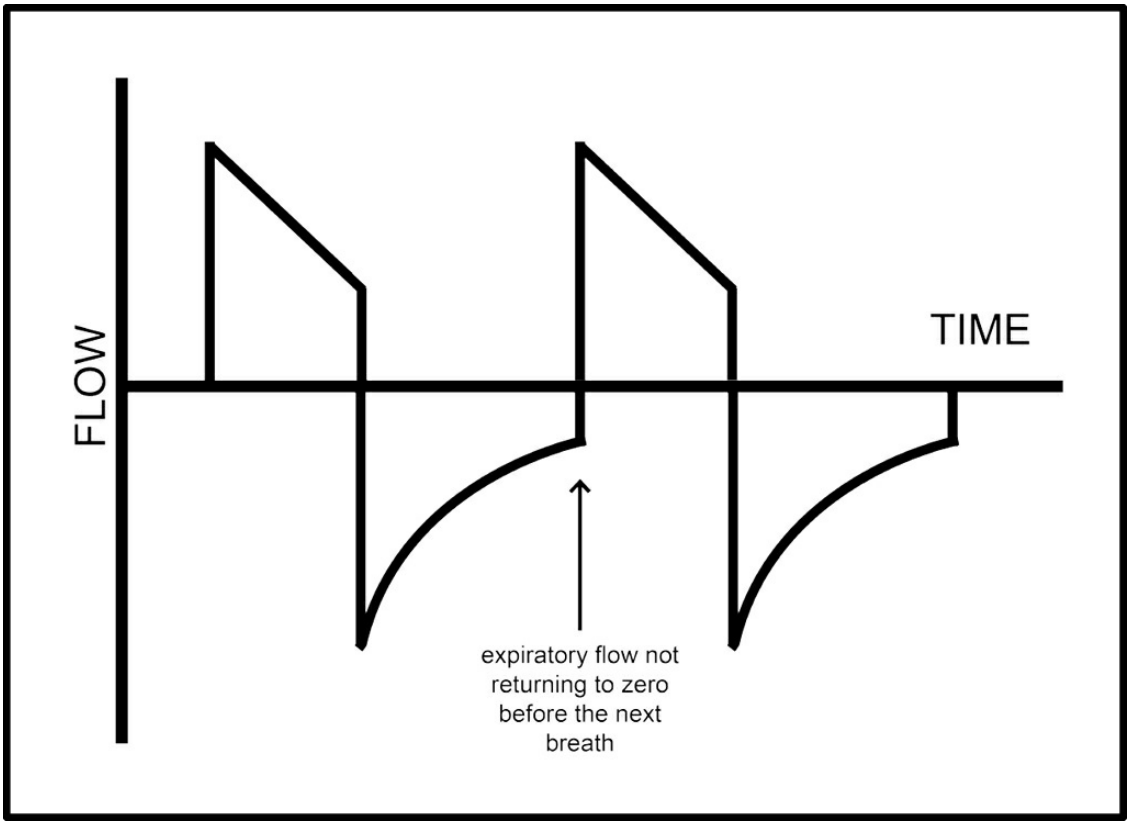


If constant flow is like drinking from a fire hose, then decelerating flow is like filling a glass of lemonade from a pitcher. Initially, the lemonade flows pretty quickly from the pitcher to the glass. As the glass fills, the pourer will lift up the pitcher gradually so that the flow of lemonade decelerates. Right as the glass becomes completely full, the flow stops. Now, imagine that the glass looks like a cast of the airways and alveoli. If you're trying to fill a complex structure with lemonade, you want to slow the flow even more to make sure all of the nooks and crannies get filled. If you extend this analogy to ventilation, it then seems that decelerating flow would result in better gas distribution to less compliant areas of lungs (which it does).

Most patients seem to tolerate decelerating flow better. Some patients, however, seem to do better with constant flow. People with COPD exacerbations or status asthmaticus often have significant air hunger and they want to get the air into their lungs quickly. Slowing the flow rate can make the dyspnea and air hunger worse.

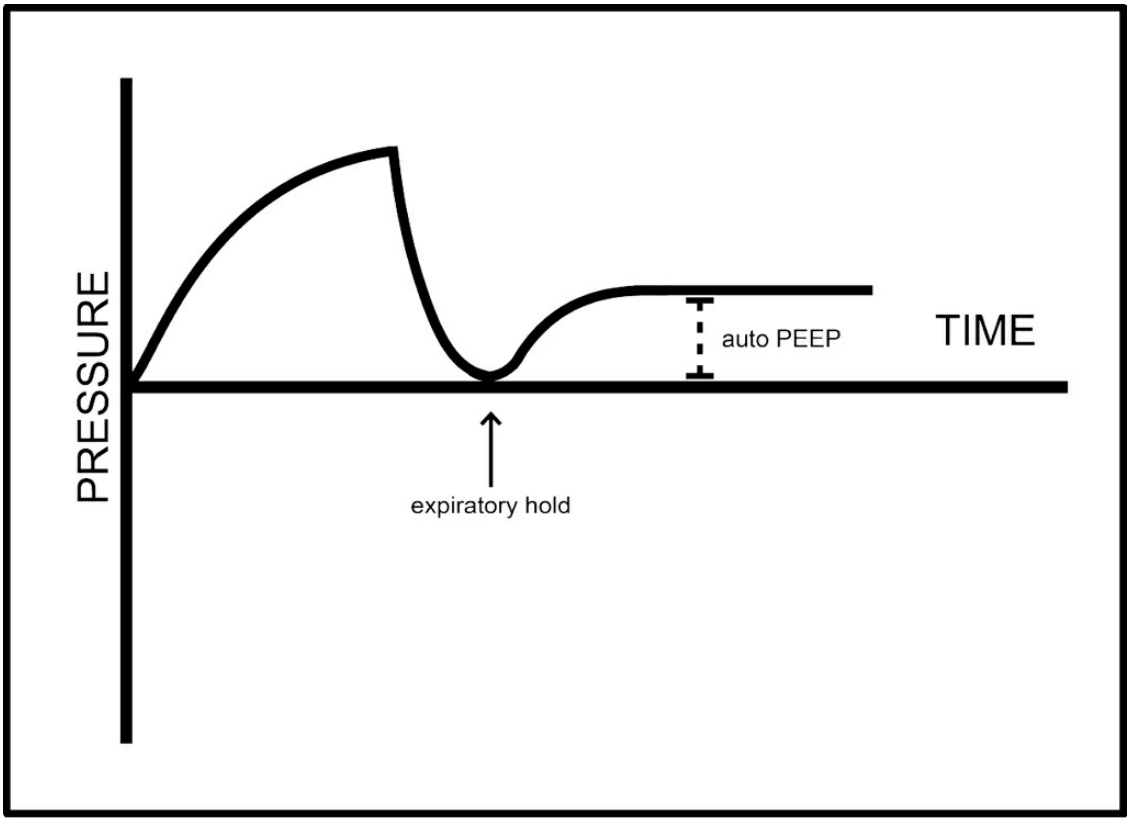
Dynamic Hyperinflation

Expiratory flow is passive and is determined by the elastance of the lungs and the airway resistance. Elastance is the reciprocal of compliance—the change in pressure over the change in volume. A lung with high elastance will recoil and empty much more quickly than one with a low elastance (or, high compliance). A stiff lung with little airway resistance doesn't take much time to empty at all—the air just rushes out. On the other hand, compliant (low elastance) lungs with high airway resistance will take much longer to empty. The latter is seen with COPD and exacerbations of asthma. Getting air into the lungs is no problem but getting air out can be difficult (due to decreased recoil, or narrow inflamed airways, or both). On the ventilator, it's important to look at the expiratory flow waveform and to make sure that the flow is coming back up to baseline, or zero. If not, then this can lead to dynamic hyperinflation (auto-PEEP). If it's severe enough, the increased intrathoracic pressures can compromise venous return to the heart.



Dynamic hyperinflation is usually evident on physical exam. The patient often appears uncomfortable, and the abdominal muscles contract during exhalation (he's trying to force the air out). Loud wheezing throughout the

expiratory phase can be heard. Neck veins may also be distended, depending on the degree of auto-PEEP. On the ventilator, you will see that the expiratory flow is not coming back to the zero baseline. If you pause the ventilator at the end of expiration (an expiratory pause maneuver) for 0.5-1.0 seconds, you can see what the alveolar end-expiratory pressure is. If it's higher than the set PEEP, then auto-PEEP is present.



The end-expiratory pressure represents the equilibration of pressures throughout the lungs when flow is stopped. This is the best assessment of the alveolar pressure. If the pressure at end-expiration exceeds the applied (set by the machine) PEEP, then there is autoPEEP present. Normally, there should be no difference between the end-expiratory pressure and the set PEEP.

When dynamic hyperinflation occurs, the ventilator should be adjusted to allow the gas to escape completely during exhalation. This may mean lowering the ventilator rate and shortening the inspiratory time. Bronchodilators and steroids can help with the airway resistance; adequate

sedation should be used to minimize agitation and tachypnea.

If the patient has COPD and auto-PEEP, you can try to splint open the conducting airways with some applied PEEP. This is possible because in COPD, the loss of recoil due to destruction of surrounding alveoli and bronchioles leads to collapse of the small airways when the expiratory flow increases. You may recall Bernoulli's Law, which says that as velocity increases, pressure decreases. This is how an airplane can fly, and it's why roofs blow off houses during tornados (the air pressure in the house is greater than the pressure outside). In this case, as airflow increases, the airways collapse because the surrounding lung parenchyma that normally holds them open has been damaged or destroyed. Splinting the airways with PEEP or CPAP helps prevent this dynamic collapse and hyperinflation.

Applying a pressure that's about 75-85% of the measured auto-PEEP will keep the airways open but still allow expiratory flow to occur.[42] This is the so-called "waterfall effect." If a river is rushing down a canyon toward a waterfall, the point at which the water goes over the falls is the critical point —very turbulent, very chaotic. If you wanted to keep the water going downstream but not have it be quite so turbulent, you would somehow have to raise the water level of the river below the falls until it was at the critical point— then, water could continue to flow down the canyon but without the chaos of the waterfall. In the analogy, the critical point is the pressure at which the small airways collapse during exhalation, trapping gas in the alveoli behind them. Raising the applied PEEP with the ventilator to about 75-85% of the alveolar pressure stabilizes the critical point—that is, it raises the river level enough to permit exhalation but not airway collapse. Increasing the applied PEEP above the alveolar pressure would have the same effect of raising the river above the height of the falls—the air would flow backwards, and the hyperinflation would worsen.

Chapter 14

Patient-Ventilator Dyssynchrony

Patient-ventilator dyssynchrony is a common problem in the ICU. Unfortunately, most of the time the patient gets the blame. He is often accused of "fighting the vent" or "bucking the ventilator," and this is used as a reason to increase the amount of sedation or even to institute neuromuscular blockade.

The first thing to do when a previously comfortable patient starts having trouble with mechanical ventilation is to make sure there's nothing wrong with the respiratory circuit. Disconnecting the patient from the ventilator and bag-ventilating him will help rule out a physiologic problem—if there's quick improvement, the issue is likely to be with the ventilator settings. If not, a focused examination to ensure that the endotracheal tube is in place, the lungs are inflated, and cardiac function is adequate is in order. The usual mnemonic is **DOPES**:

- Displacement of the endotracheal tube (recognized by loss of the end-tidal CO_2 waveform)
- Obstruction of the endotracheal tube, or of the airways (loss of the $ETCO_2$ waveform with complete obstruction, high airway resistance with partial obstruction leading to wheezing or a "shark fin" appearance of the $ETCO_2$ waveform)
- Pneumothorax
- Equipment malfunction
- Stacking of breaths

Additionally, be on the lookout for things like pulmonary embolism, sepsis, delirium, fever, and other causes of agitation.

Once you are satisfied that there is not a problem with the patient, it's

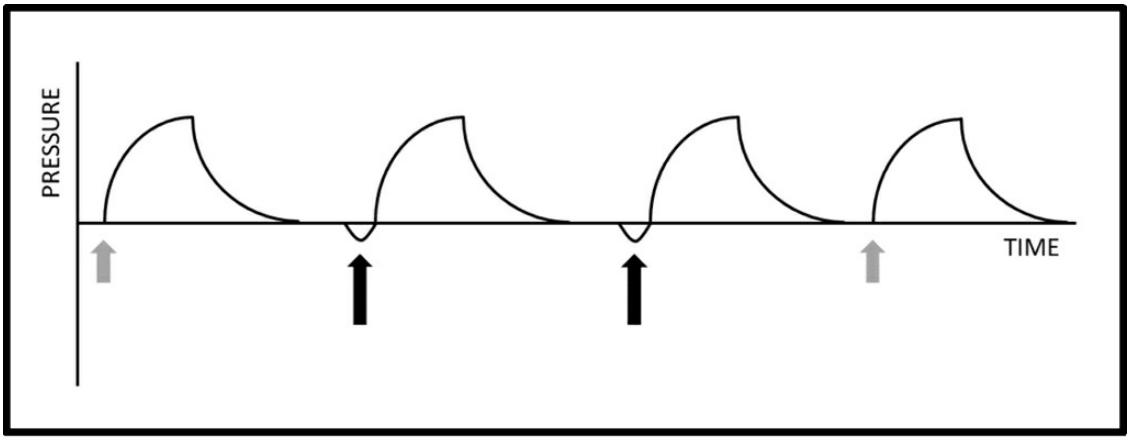
time to turn your attention to the ventilator. While there are many reasons for patient-ventilator dyssynchrony, the major causes can be grouped into:

- Ineffective or inappropriate triggering of the ventilator
- Inadequate inspiratory assistance
- Inappropriate termination of the breath

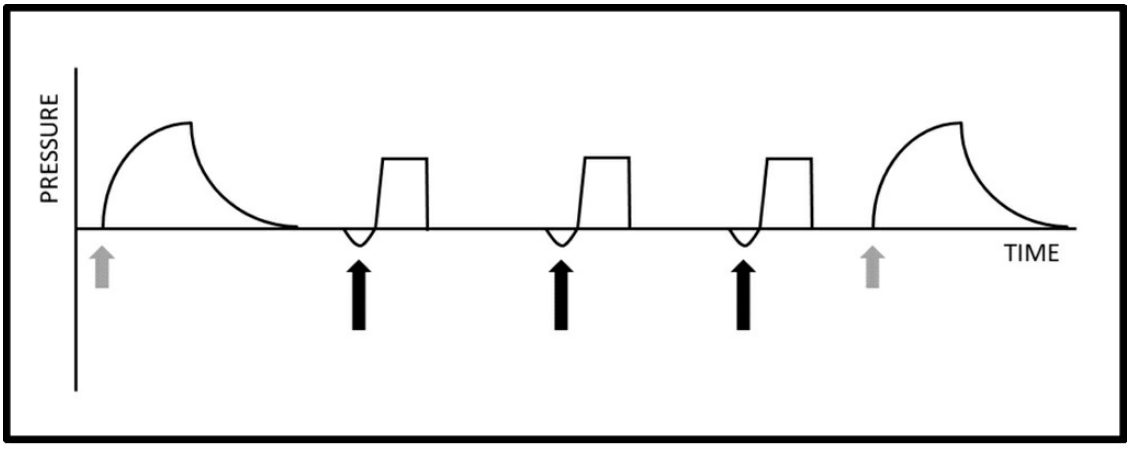
Ineffective or inappropriate triggering

Triggering the ventilator occurs when the patient makes an effort to signal the ventilator that he wants a breath. In almost every mode of ventilation used in clinical practice, the patient is never “locked out” of the vent. Controlled mandatory ventilation (CMV), where the rate is set by the machine and the patient cannot breathe over the set rate, is used in operating rooms under conditions of general anesthesia. In the intensive care unit, however, ventilators are set to allow patient-initiated breaths above the set rate.

The trigger can be set to use either a negative inspiratory pressure (usually -1 to -3 cm H_2O) or an inspiratory flow rate (usually 1 to 4 L/min). When this is actuated by the patient, the ventilator delivers what the mode prescribes. In assist-control ventilation, the response to a patient-triggered breath is either the tidal volume (in volume assist-control) or the inspiratory pressure for the duration of the inspiratory time (in pressure assist-control). In pressure support ventilation or SIMV, the patient’s effort leads to a predefined inspiratory pressure that is maintained until the inspiratory flow drops to a certain threshold (usually 25-30% of the peak flow), at which time the breath is terminated.



Triggering in Volume Assist-Control ventilation. The grey arrows indicate machine-triggered breaths. The black arrows show the slight negative pressure generated by the patient. This is followed by a fully supported breath delivered by the ventilator.

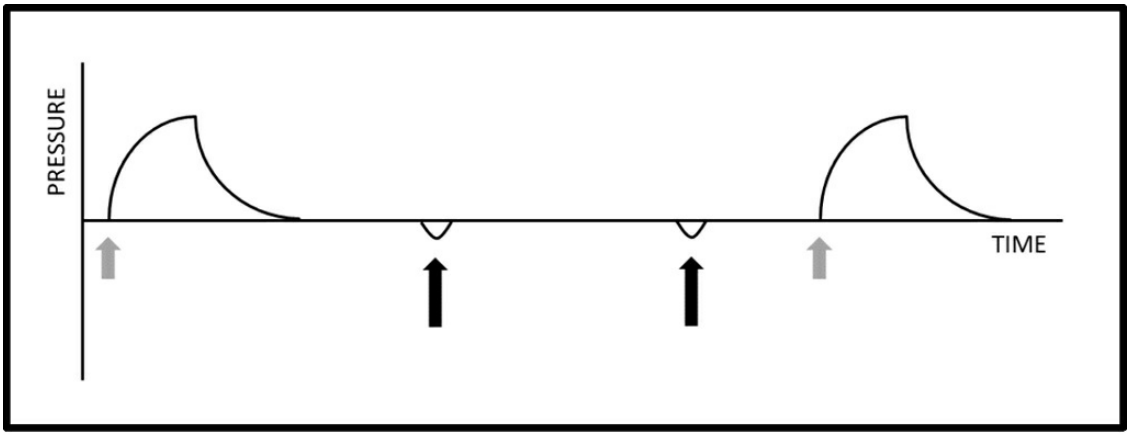


Triggering in SIMV/PS ventilation. The grey arrows indicate machine-delivered breaths, which are delivered based on the set rate. The black arrows show patient-triggered breaths, which are pressure-supported.

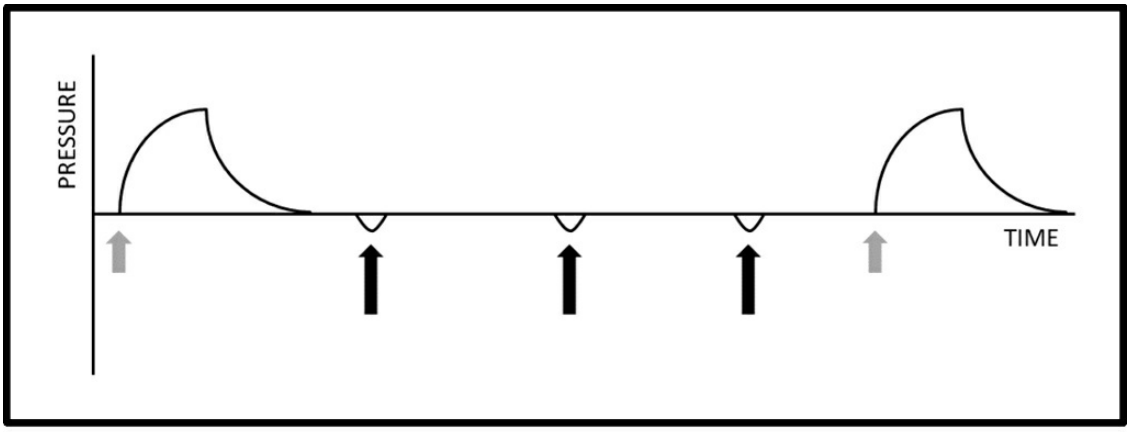
Ineffective triggering occurs when the patient makes an effort to breathe but the ventilator does not respond. This can be due to something as simple as too stringent of a trigger setting—check the ventilator and adjust the inspiratory pressure or flow trigger as needed to allow the patient to trigger

the ventilator effectively. More often, however, the setting on the ventilator is appropriate but the patient cannot trigger due to either hyperinflation (autoPEEP) or neuromuscular weakness.

The most accurate way to diagnose ineffective triggering is with the use of an esophageal balloon catheter. When placed in the mid-esophagus, the pressure transduced by the catheter reflects the average intrapleural pressure. Dips in the pressure waveform represent spontaneous respiratory efforts, which lower the pleural pressure and create a negative pressure at the level of the endotracheal tube. This should signal to the ventilator that the patient wants a breath.



Ineffective triggering during Volume Assist-Control ventilation. The black arrows indicate patient effort, but the attempt to trigger the ventilator doesn't result in delivery of a breath. The ventilator is providing breaths according to the set machine rate (grey arrows).



Ineffective triggering during SIMV/PS ventilation. The patient's efforts (black arrows) do not result in a pressure-supported breath. The machine breaths (grey arrows) are delivered according to the set machine rate.

If the patient has a significant amount of autoPEEP due to obstructive airways disease like COPD or asthma, the increased alveolar pressure at end-expiration serves to effectively increase the threshold required to signal the ventilator beyond what the set trigger is. For example, a patient with a measured end-expiratory alveolar pressure of 10 cm H_2O (with zero applied PEEP) has to generate *12 cm* of intrapleural pressure to reach a negative airway pressure of -2 cm H_2O. If the trigger on the ventilator is set at -2 cm, considerable respiratory effort will be required for the patient to breathe over the set ventilator rate.

Most ICU patients don't have an intraesophageal balloon catheter. Nevertheless, diagnosing ineffective triggering isn't that difficult. Look at the pressure waveform on the ventilator. If negative deflections that aren't followed by a breath are present, place your hand on the patient's abdomen. If you feel the abdominal wall pulling down but no breath follows this effort, then ineffective triggering is present. Check the end-expiratory alveolar pressure to measure autoPEEP. If autoPEEP is present, then try to correct it by extending the expiratory time and by treating airway obstruction (bronchodilators, steroids, airway clearance maneuvers).

Occasionally, a patient may not be able to trigger the ventilator due to neuromuscular weakness. This can be seen in primary neuromuscular diseases like myasthenia gravis and Guillain-Barre syndrome, or with ICU-

acquired weakness. Changing from a pressure trigger to a flow trigger may be helpful. Use a lower-threshold trigger setting if possible.

One solution to ineffective triggering is the use of neurally adjusted ventilator assist (NAVA™). With NAVA, an esophageal catheter with electrodes is placed so the electrodes can detect electrical activity during diaphragmatic stimulation by the phrenic nerves. When the electrical stimulus is detected, the ventilator initiates a breath. The amount of support can be set by the clinician—typically, the NAVA level (cm $H_2O/\mu V$) is multiplied by the electrical sensitivity threshold (usually 0.5 μV) to get the positive pressure required for a tidal volume of 6-8 mL/kg. When the ventilator detects diaphragmatic activity, the NAVA support is maintained until the electrical signal falls by 50-75%. The support provided by the ventilator depends on the strength of the diaphragmatic electrical activity, and therefore the pressure delivered is variable. The coordination between diaphragmatic contraction and breath delivery also reduces the delay between patient triggering and ventilator response. This should, theoretically, improve patient-ventilator synchrony.

Flow Starvation

Sometimes, the ventilator doesn't deliver the inspired gas as quickly as the patient would like it. This can cause considerable discomfort—imagine if, after running around a track as quickly as you could, I forced you to breathe through a narrow tube. On the ventilator, this is appropriately termed "flow starvation."

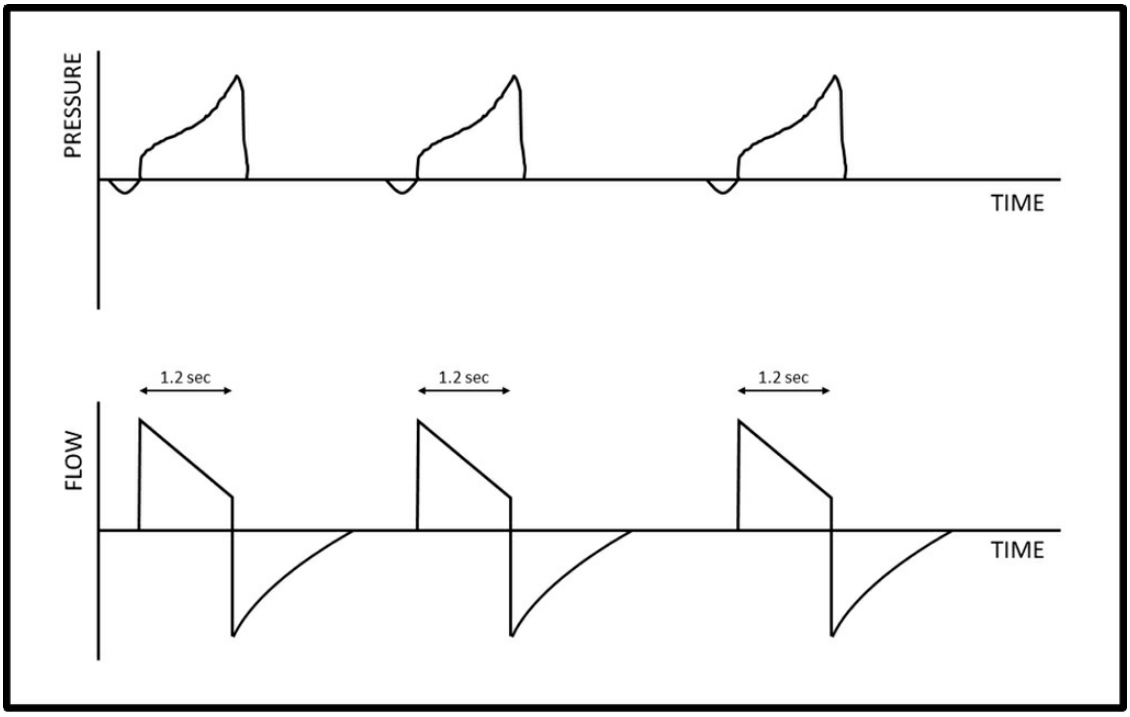
During flow starvation, the inspiratory flow is less than what the patient requires. This can occur if the flow is set to decelerate as the breath is delivered or if the inspiratory rise time is too long. On the pressure-time chart, the inspiratory pressure waveform has a scooped-out appearance, due to the patient's inspiratory effort— it's like he's trying to suck in the air forcefully. Flow starvation can also lead to double triggering of the ventilator, which will be discussed later in this chapter.

The solution to flow starvation? Provide more flow. This can be done a few different ways:

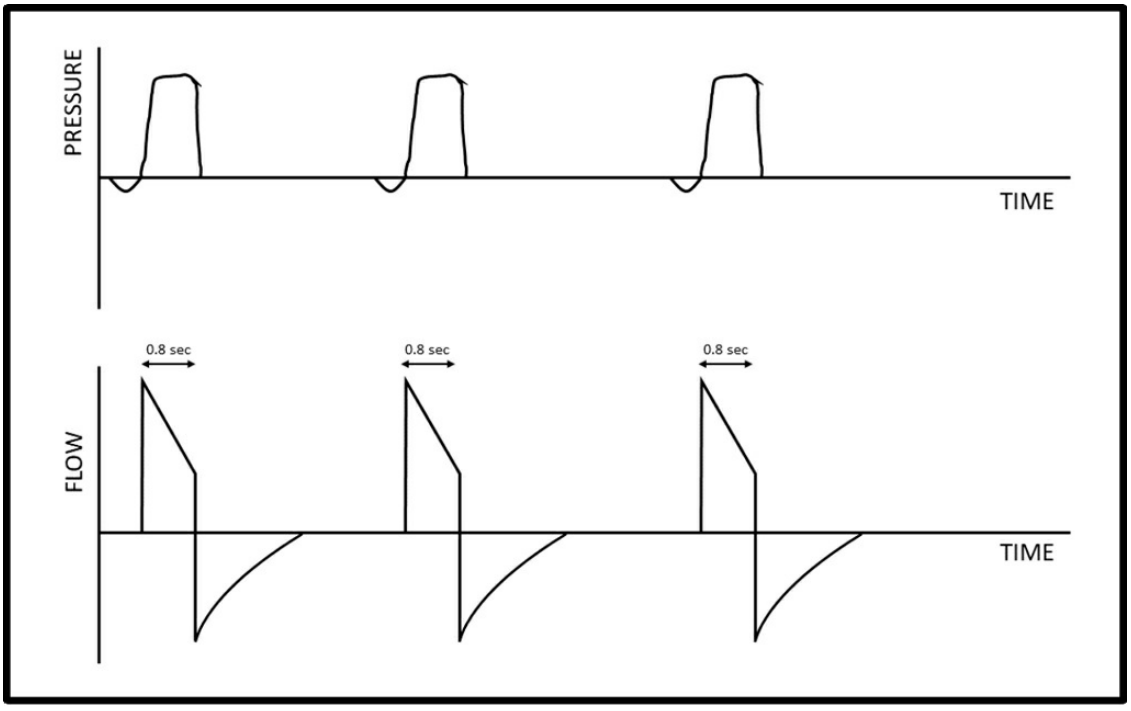
- Shorten the inspiratory time (I-time), if the ventilator mode is volume control. Especially in dual-control modes like PRVC and VC+ and

Autoflow, the ventilator is set to deliver the preset tidal volume in a specified inspiratory time. The ventilator then adjusts the deceleration of the inspiratory flow to get the tidal volume delivered using the lowest pressure possible. Most of the time, this is a good thing and is more comfortable for the patient. If flow starvation is present, however, it could mean that the ventilator is taking too long to give him the volume of gas he wants. Shortening the I-time will automatically increase the flow rate needed to deliver the tidal volume.

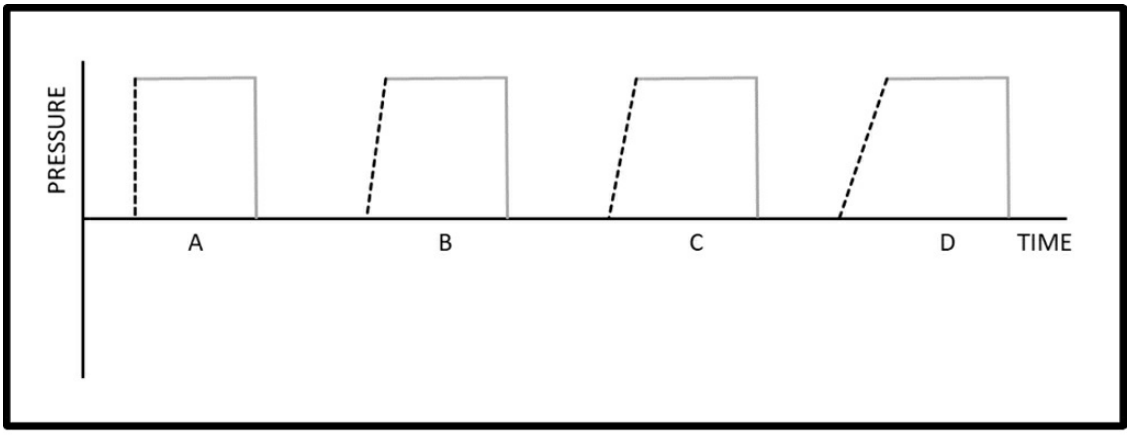
- Change the flow from decelerating to constant. Most patients prefer decelerating flow, but when there's a lot of air hunger (especially in patients with COPD or asthma), constant inspiratory flow gets the desired volume of gas delivered faster.
- Shorten the inspiratory rise time. This usually doesn't affect things much, but if you're trying to fine-tune the ventilator to match the patient's needs, it is something to look at. The rise time refers to the time it takes for the ventilator to go from zero flow to peak inspiratory flow. If the rise time is too long, the patient may feel like the ventilator is slow to meet his inspiratory demand. If the rise time is too short, then it may feel like breathing from a compressed air hose. The usual rise time is 0.1-0.15 seconds.



Flow starvation during Pressure-Regulated Volume Control, as seen in the concave scoop on the pressure-time graph. This patient's inspiratory time is 1.2 seconds. This, coupled with the decelerating inspiratory flow, can lead to flow starvation if the patient has considerable air hunger or needs a high minute ventilation to meet his metabolic demands.



In the same patient, the inspiratory time has been shortened to 0.8 sec. This gets the prescribed tidal volume delivered in a shorter time, which necessarily increases the inspiratory flow necessary. The pressure-time waveform has a more normal appearance, indicating that the flow starvation has been corrected.



The rise time is the time it takes for the airway pressure to reach its peak value and is reflected by the dashed line.

A: Rise time of 0.0 seconds. This would be appropriate for a patient with considerable air hunger.

B: Rise time of 0.1 seconds. This is appropriate in most patients.

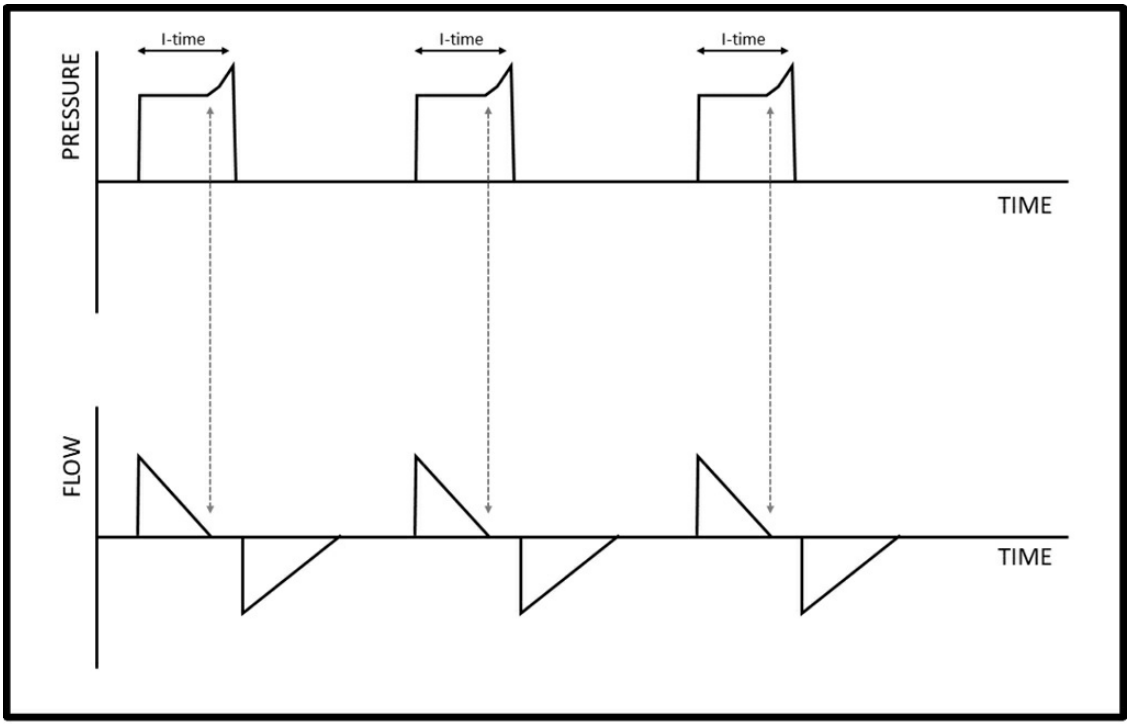
C: Rise time of 0.15 seconds. Again, this is appropriate in most patients, but it means that the initial gas delivery is not quite as abrupt as in B or A.

D: Rise time of 0.25 seconds. This is prolonged and can lead to flow starvation. A prolonged rise time can be appropriate in a patient with severely reduced respiratory compliance where there is a desire to keep the inspiratory pressures lower.

Too Long of an Inspiratory Time

When the compliance of the patient's respiratory system is low, a "normal" inspiratory time may be too long. This is evident on the flow-time waveform—the inspiratory flow returns to zero, and then there's a pause before expiratory flow begins. This is not necessarily a bad thing, especially if alveolar recruitment is the goal. The end-inspiratory pause serves to recruit collapsed alveoli and to improve the end-inspiratory lung volume. Sometimes, however, the patient might not like this and tries to exhale during

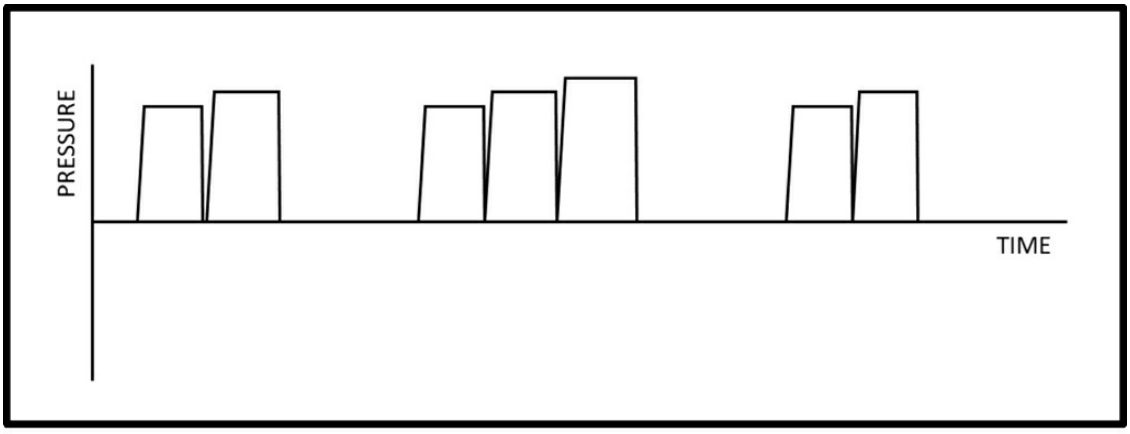
the inspiratory time. This will be seen on the pressure-time waveform as an upward deflection at the end of inspiration, and as a sharp expiratory flow wave. The solution, obviously, is to shorten the inspiratory time.



In this patient, the inspiratory time is too long. The inspiratory flow has stopped because the lungs are full and the patient is trying to exhale, but the ventilator is set to maintain the inspiration for 1.2 seconds. The solution is to reduce the inspiratory time.

Double Triggering

Double triggering is one of the most common problems encountered in the ICU and it can be due to several factors. Double *triggering* is the term used when the patient initiates the breath(s), as opposed to double (or auto) *cycling*, which is when the problem is in the ventilator circuit itself, or with the patient but not related to inspiratory effort.



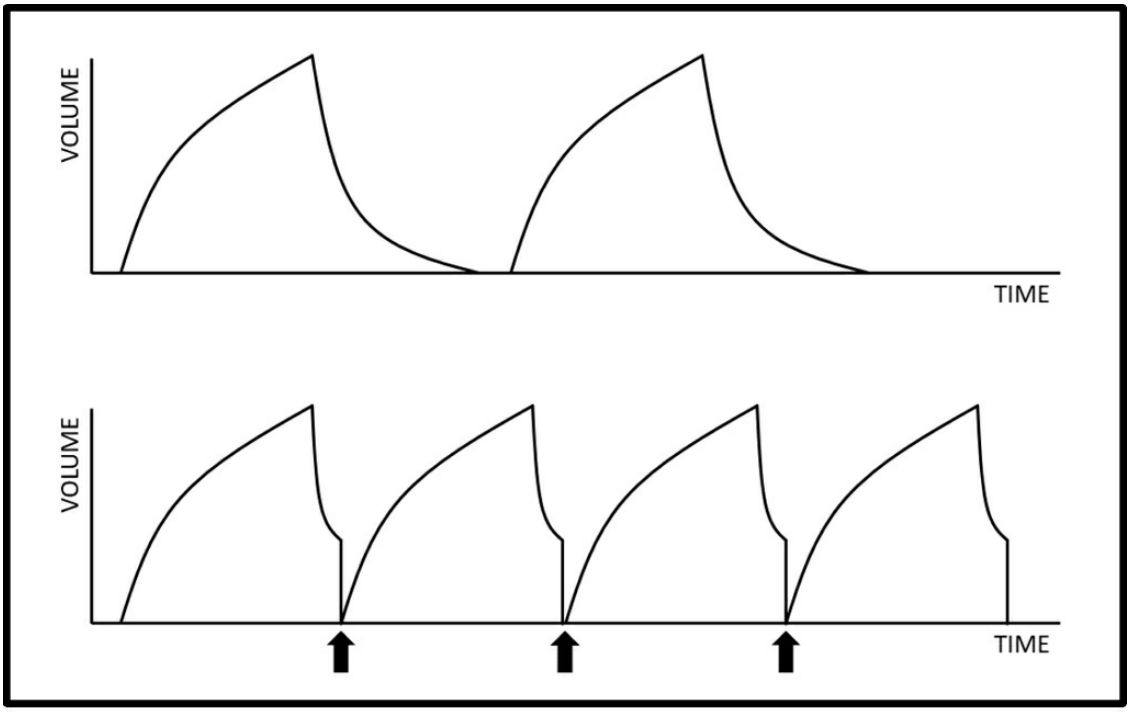
Double- and triple-cycling of the ventilator.

Basically, double triggering occurs when the ventilator senses that the patient wants another breath, even when he's just triggered the vent. This leads to breath stacking—2, 3, or 4 breaths in a row. The solution depends on the cause. Many times, it takes trying a few things before a solution is found. Here are some of the reasons for double triggering:

- The trigger is too sensitive—lower the sensitivity or change from pressure to flow trigger (or vice versa).
- The patient wants more volume than what you're giving him. This often happens when a spontaneously breathing patient has a "lung-protective" tidal volume of 4-6 mL/kg in volume assist-control mode. The ventilator turns off the gas when the set volume has been delivered, but the patient keeps breathing in. The ventilator interprets this as another respiratory effort and delivers another tidal volume right after the first one. The solution is to either:
    - Increase the tidal volume—while this is probably the best, and easiest, thing to do, it runs afoul of standardized ventilator protocols and can lead to chastising emails.
    - Change to pressure assist-control mode—this guarantees the patient the inspiratory pressure, with a variable tidal volume. Adjust the inspiratory time to ensure that the inspiratory flow comes close, or to, baseline.
    - If you want to control the tidal volume, switch to SIMV with pressure support. The patient's spontaneous breaths will be

boosted by the PS, while there's still a set rate and tidal volume that he's guaranteed to receive.

- Check the circuit for auto cycling. As stated above, auto cycling happens when there's a problem with the patient or in the ventilator circuit causing the machine to deliver breaths repeatedly. Common reasons for auto cycling:
    - Leaks in the circuit—look carefully and fix as appropriate.
    - Condensation in the ventilator tubing—as the water sloshes back and forth, it can trigger the ventilator. Change the tubing to fix it.
    - A bronchopleural fistula with a significant air leak can trigger the ventilator—solutions include lowering the trigger sensitivity (and using pressure instead of flow) or using high frequency oscillatory ventilation.
    - Rarely, pacemaker spikes can be a vigorous enough stimulus to trigger the ventilator. It's also been reported with intra-aortic balloon counterpulsation. Adjusting the ventilator trigger should help the problem.



In the top waveform, the volume is returning to zero at the end of each breath, which is normal. In the bottom waveform, there is an abrupt drop to zero before the termination of the breath (black arrows). This can be seen when there is a leak in the ventilator circuit, but it is more commonly seen with a bronchopleural fistula and a high-output air leak from the chest tube. In this example, the drop in volume is enough to auto-trigger the ventilator. Another clue that this is the cause would be large discrepancy between the inspired and expired volume on the ventilator.

Chapter 15

Severe Bronchospasm and Hyperinflation

Mechanical ventilation of patients with severe bronchospasm can be very difficult. This usually occurs with status asthmaticus, but it can also be seen with respiratory failure due to chronic obstructive lung disease, inhalation of toxic fumes, and viral bronchiolitis. Status asthmaticus in particular can be tough to treat due to the combination of bronchospasm and mucus plugging, which significantly worsens ventilation-perfusion matching.

For those patients with bronchospasm requiring mechanical ventilation, it is important to differentiate high airway resistance from high alveolar pressure. This can be done by performing an inspiratory pause maneuver on the ventilator. At the end of inspiration, flow is temporarily stopped for 0.5 to 1.0 seconds. During this time, pressures will equilibrate across the respiratory system. The pressure in the endotracheal tube will be the same (or nearly so) as the pressure in the alveoli. This is known as the plateau pressure (P_{PLAT}). The difference between the peak inspiratory pressure (PIP) and the P_{PLAT} is an estimate of the airway resistance. Normally, the gradient between the PIP and P_{PLAT} is 5 cm or less. If the gradient is higher, then the resistance to flow is elevated. This can be due to an issue with the endotracheal tube— if it's a small-diameter tube, or if it's kinked, or if it's partially plugged with mucus, the airway resistance will rise. If the tube is functioning well, is properly sized, and not obstructed, then a high airway resistance usually means that there's bronchospasm present (even if wheezing can't be auscultated). Treatment with inhaled beta-agonists and anti-muscarinics may help.

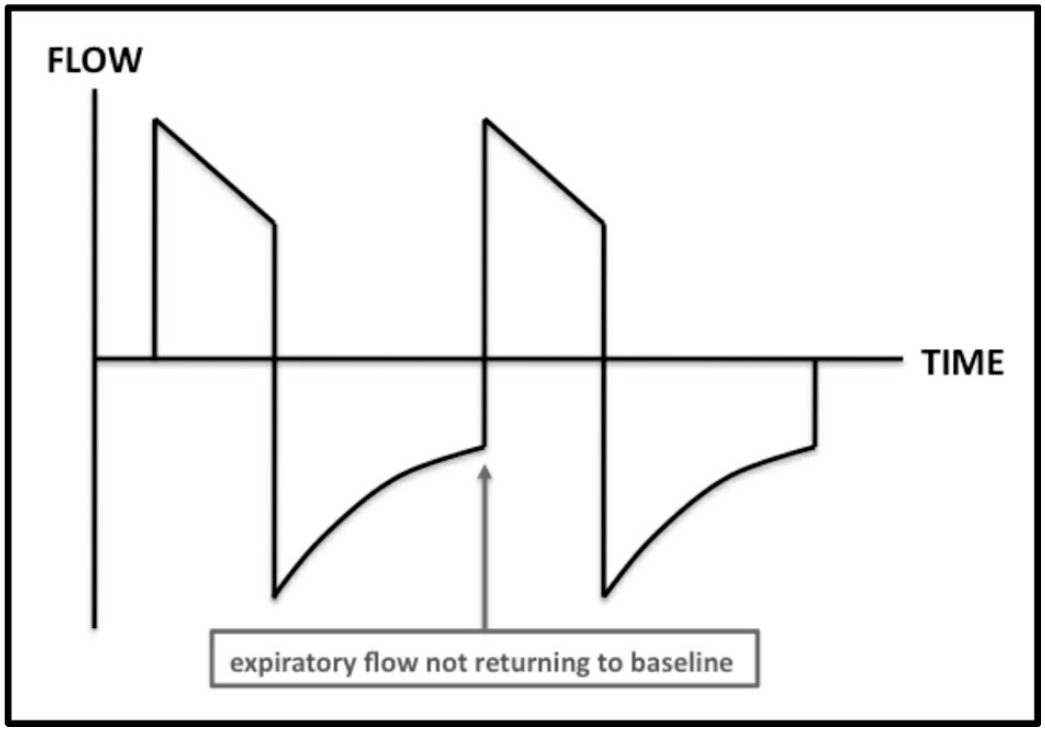
If the PIP and P_{PLAT} are both elevated, especially if the P_{PLAT} is over 30 cm H_2O, then it indicates increased alveolar pressure. Common situations that increase the alveolar pressure include mainstem intubation (all the

volume for two lungs is going into one); pneumothorax; pulmonary edema; mucus plugging leading to atelectasis; dynamic hyperinflation; and increased abdominal pressure. While all of these can occur in any patient requiring mechanical ventilation, asthmatics are especially prone to mucus plugging, dynamic hyperinflation, and pneumothorax. These should definitely be considered in any ventilated asthmatic who suddenly gets worse.

Dynamic hyperinflation can be diagnosed both on the ventilator and by physical exam. On examination, the patient will usually appear uncomfortable. Paradoxical breathing, with the chest and abdomen moving in a dyssynchronous manner, can be seen. On auscultation, loud wheezing can be heard right up until the next breath is delivered. The cardiac monitor may display lower voltage of the QRS complex during inspiration, due to the trapped gas in the thorax impeding the electrical current. If the patient has an arterial line, pulsus paradoxus* may be present. The patient's jugular veins may be distended during expiration but collapse during inspiration, owing to the increased intrathoracic pressure at the end of expiration.

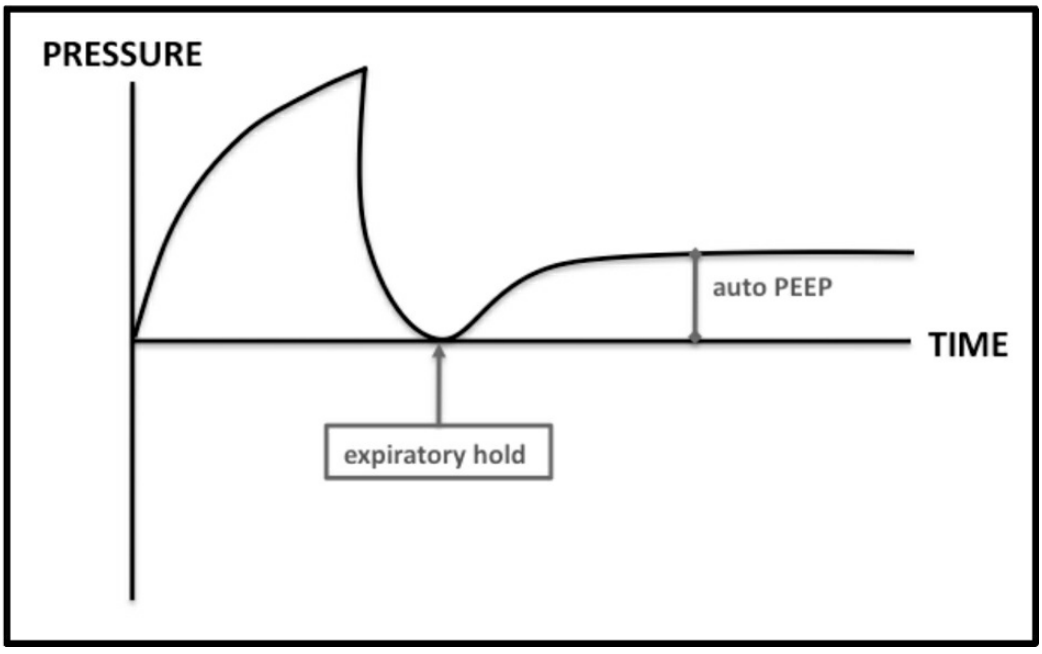
On the ventilator, dynamic hyperinflation can be observed by looking at the expiratory flow-time waveform. Normally, at end-expiration the flow should be zero. All of the gas has escaped, leaving the lungs at functional residual capacity. With dynamic hyperinflation, there is usually some expiratory gas flow ongoing at the time of the next inspiration. This may not always be present, however, and so an expiratory pause maneuver should be performed if dynamic hyperinflation is suspected.

Dynamic Hyperinflation



The mechanics behind the expiratory pause maneuver are similar to the inspiratory pause—when flow stops, pressure equilibrates. This time, the pressure is equilibrating at the end of expiration, when alveolar pressure should normally be zero. If any PEEP is set on the ventilator, the alveolar pressure should equal the PEEP. With dynamic hyperinflation, the actual (or measured) end-expiratory pressure will be higher than the applied (or set) PEEP. This is why dynamic hyperinflation is often referred to as “auto-PEEP.”

Expiratory Hold Maneuver Demonstrating Auto-PEEP



Ventilator Management

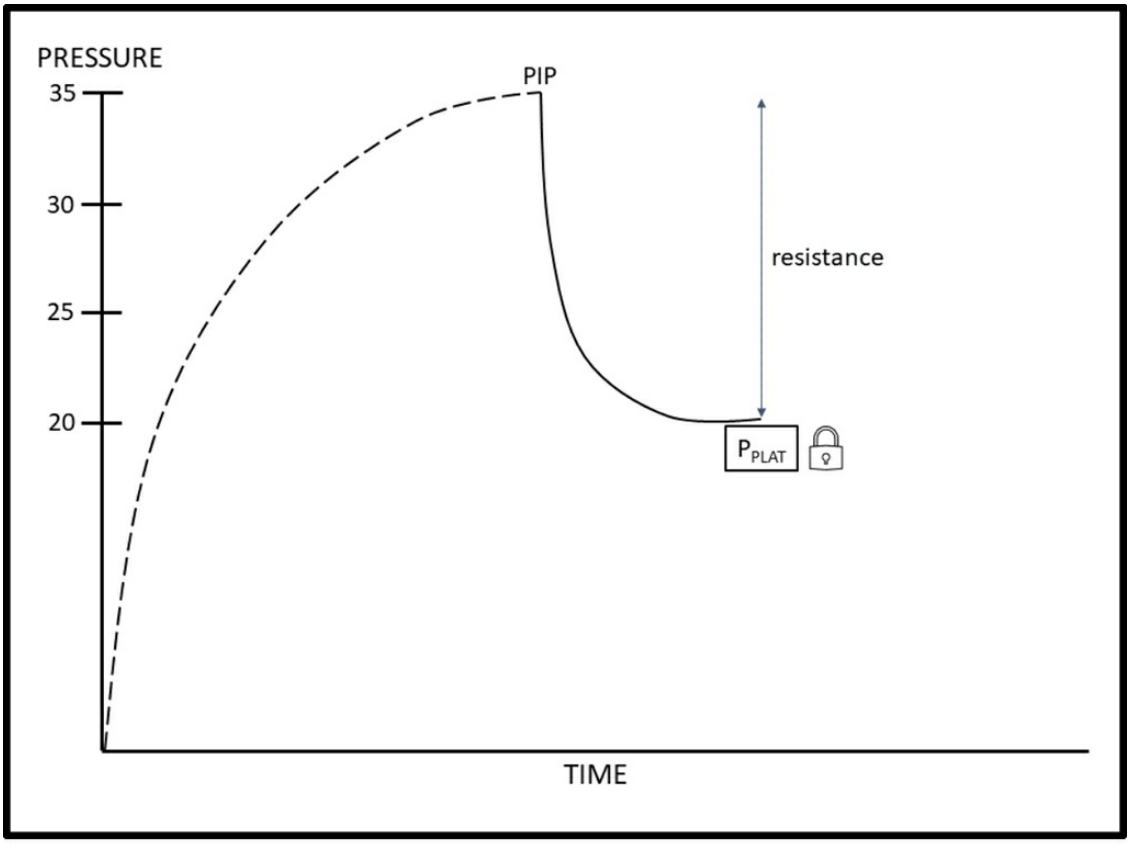
The goals with mechanical ventilation in the patient with severe bronchospasm are to minimize hyperinflation, allow the respiratory muscles to rest, and to avoid complications like pneumothorax, pneumomediastinum, and pulmonary interstitial emphysema. With regard to gas exchange, the goal is adequate (not perfect) oxygenation and toleration of hypercapnic acidosis.

Dynamic hyperinflation can be minimized by simply giving the patient enough time to exhale completely. This can be done by lowering the respiratory rate and/or reducing the inspiratory time (the time it takes for the breath to be delivered). Of the two, lowering the respiratory rate is the most effective. Consider a patient with a respiratory rate of 20 and an inspiratory time (I-time) of 1 second. With 20 breaths per minute, there are 3 seconds allocated per breath. The I-time is set at 1.0 seconds, leaving 2.0 seconds for expiration. The ratio between inspiration and expiration time is thus 1:2. If the clinician wants to permit more time for expiration, he can shorten the inspiratory time and prolong the I:E ratio. In this example, if the I-time is lowered to 0.7 seconds, there are now 2.3 seconds left for expiration. This translates to an I:E ratio of 1:3.3. This is better, but it may not be sufficient to permit adequate expiration through narrowed, inflamed airways. You will

also find that shortening the inspiratory time by too much can cause a good bit of air hunger and discomfort, as well as very high peak inspiratory pressures. In turn, this can lead to heavy sedation and neuromuscular blockade. Try taking in your breaths in 0.5 seconds—you won't like it for long.

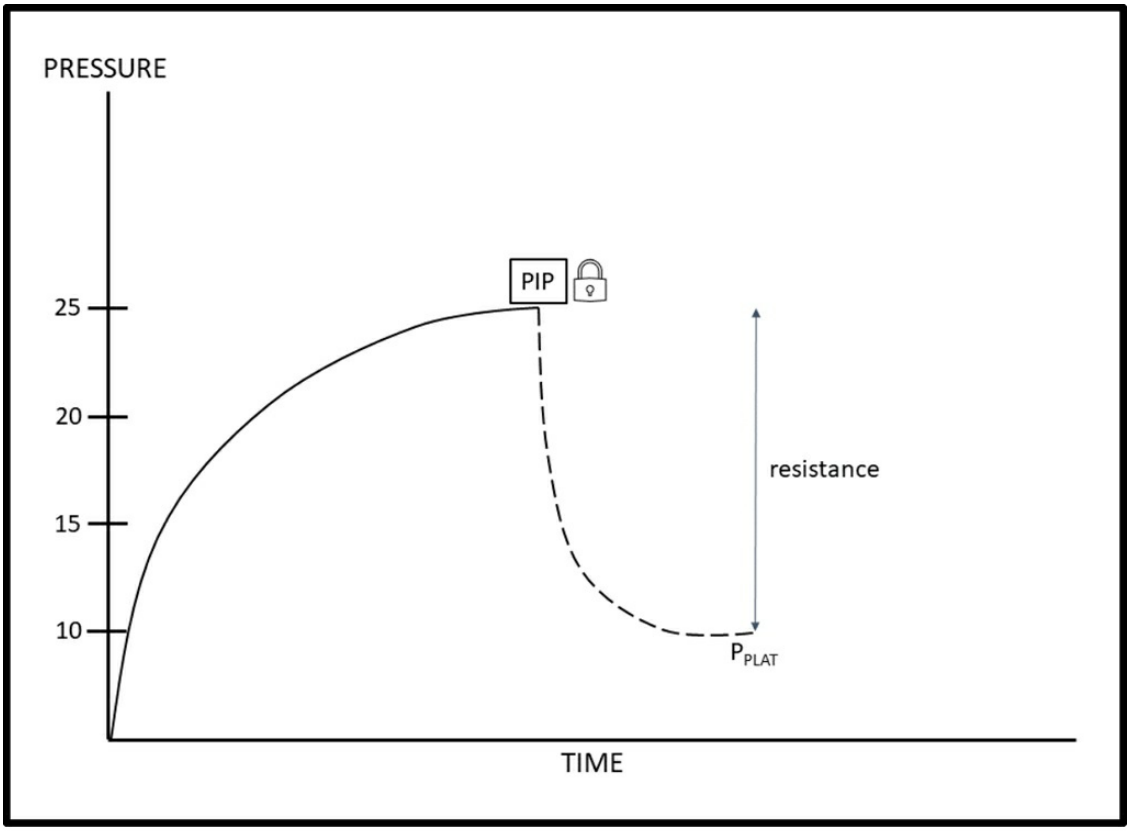
Lowering the respiratory rate is the more effective way of prolonging the I:E ratio while minimizing patient discomfort. In the example above, if we lower the respiratory rate to 15, there are now 4 seconds per breath. If the I-time is kept at 1.0 second, the expiratory time is 3.0 seconds. The I:E ratio is 1:3. Lower the respiratory rate to 12, and the I:E ratio is 1:4. A rate of 10—the I:E ratio is 1:5. Most of the time, there isn't much benefit to an I:E ratio any longer than 1:5.

The mode of choice in most cases of severe bronchospasm (and any time airway resistance is significantly increased is *volume control ventilation*. Pressure control can be very risky. Remember that with volume control ventilation (VCV), you set a tidal volume that the patient is guaranteed to receive. This is linked to the alveolar pressure (P_{PLAT}) by the static compliance of the lung. In effect, you are "fixing" the tidal volume and the end-inspiratory alveolar pressure. If airway resistance worsens, the ventilator will have to increase the total inspiratory pressure (PIP) in order to get to the goal tidal volume/P_{PLAT}.



With VCV, the tidal volume and end-inspiratory alveolar pressure (P_{PLAT}) are "locked in." That means that the peak inspiratory pressure will go up or down depending on the airway resistance. This guarantees consistent alveolar ventilation, as long as the PIP doesn't exceed the alarm settings on the ventilator.

With pressure control ventilation (PCV), on the other hand, the PIP is fixed. The ventilator will not exceed this, so if the airway resistance increases then the P_{PLAT} will have to drop (recall that the PIP is the sum of the P_{PLAT}, the end-inspiratory alveolar pressure, and the pressure needed to overcome the resistance of the airways). This can rapidly lead to sudden and severe alveolar hypoventilation. The risk is compounded by the fact that if PCV is the mode of choice, the typical warning for high airway resistance (high airway pressure alarm) will not sound. Instead, clinicians will need to look for the low tidal volume or low minute ventilation alarm to know that the airway resistance has increased.



With PCV, the PIP is "locked in." Since the PIP is the sum of the P_{PLAT} and the pressure needed to overcome the airway resistance, any increase in resistance has to be offset by a reduction in the P_{PLAT}. This can push the P_{PLAT} (and thus, the tidal volume) dangerously low.

Low tidal volumes can also work against the patient with severe bronchospasm, especially if he isn't heavily sedated. Air hunger is a common symptom of an exacerbation of asthma or COPD, and low tidal volumes can make the patient very tachypneic. A tidal volume of 6 mL/kg predicted body weight (PBW) is great for ARDS, but with asthma and COPD, a higher tidal volume is often needed. 8 mL/kg PBW usually works without causing overdistension, and it mitigates the tachypnea and air hunger. Higher tidal volumes, especially > 10 mL/kg PBW, do increase the risk of barotrauma.

Initial Ventilator Settings for Severe Bronchospasm

- **Mode: Volume Assist-Control Ventilation**
- **Rate: 10-14 Breaths/minute**
- **Adjust Inspiratory Time to keep I:E ratio 1:3—1:5**
- **Constant inspiratory flow**
- **Tidal Volume: 8 mL/kg PBW**
- **PEEP: zero (or ZEEP)[*]**
- **FiO_2: 100% to start, adjusted downward to keep SpO_2 8895%**

The concept of permissive hypercapnia is very important when caring for patients with severe bronchospasm. The idea is that preventing lung injury (in the form of dynamic hyperinflation or barotrauma) is more important than having normal gas exchange. Maintaining adequate oxygenation is important —keep the SpO_2 88-95%, and the PaO_2 55-80 mm Hg. The $PaCO_2$ is less important, unless there is a significant coexisting condition like increased intracranial pressure that precludes permissive hypercapnia. In general, as long as the pH is kept above 7.10, it's all right to allow the $PaCO_2$ to rise. Buffer therapy such as sodium bicarbonate infusions can also be used to keep the pH above this threshold. The adoption of permissive hypercapnia seems to be associated with a significant decline in the mortality seen with status asthmaticus and mechanical ventilation.[43]

Pharmacologic Management

Respiratory care of the patient with severe bronchospasm begins with treatment of the underlying condition. Asthma and COPD exacerbations are treated with inhaled beta-adrenergic agonists like albuterol; inhaled antimuscarinics like ipratropium bromide; and systemic corticosteroids. The dosing of corticosteroids depends on the disease in question and the underlying pathophysiology. Asthma has a strong allergic component and is associated with inflammation and airway hyper-responsiveness. Initial dosing of corticosteroids in the ICU should be 1-2 mg/kg of prednisone (or

equivalent) daily. The bronchospasm in COPD, on the other hand, is more related to excessive mucus production and narrowing of airways due to dynamic collapse during forced exhalation. It has much less of an inflammatory component when compared with asthma. Lower dosing of prednisone (or equivalent) is appropriate. Most studies suggest that there is little benefit from a prednisone dose in excess of 40-60 mg per day for COPD exacerbations, and there is always the potential for harmful effects from higher doses. Corticosteroids do not have a linear dose-response relationship in respiratory illness—doubling the steroid dose will not halve the bronchospasm.

In addition to corticosteroids and inhaled bronchodilators, adequate sedation and analgesia are important. The discomfort of the endotracheal tube, along with the tachypnea associated with an exacerbation of pulmonary disease, can lead to air trapping and hyperinflation. Narcotic analgesia (like a fentanyl infusion) minimizes the discomfort of the tube and other devices and helps take away the subjective feeling of breathlessness. Titratable sedatives such as propofol and dexmedetomidine may also be helpful. Use of a sedation scale, such as the Richmond Agitation-Sedation Scale (RASS), is important for nursing staff to titrate the sedation. In my experience, titration to a RASS of -1 to -2 is effective in patients with severe bronchospasm. Neuromuscular blockade can be used if the patient-ventilator dyssynchrony is severe or if the dynamic hyperinflation is causing significant hemodynamic instability. It should be used sparingly and only until the patient stabilizes, however, due to the higher risk of critical illness-associated weakness with these drugs (especially when corticosteroids are also administered, as they usually are). Of the neuromuscular blockers available, cisatracurium is preferred due to its metabolism not being affected by renal or hepatic dysfunction.

Ketamine is a dissociative agent that has marked sedative and analgesic properties, and it’s most commonly used for procedural sedation. Unlike benzodiazepines, which act on inhibitory GABA receptors, ketamine blocks excitatory NMDA receptors in the central nervous system. NMDA receptors are also present in the lungs and appear to play a role in bronchoconstriction. Ketamine’s anti-NMDA effect would therefore make it an attractive agent to use in conditions of severe bronchospasm like status asthmaticus. Experimental models have also suggested that ketamine has a salutary effect on bronchospasm through effects on norepinephrine reuptake and vagal

inhibition.[44]

Ketamine is not without side effects. The most commonly reported is an increase in airway secretions. Psychiatric side effects have also been described, including disorientation and hallucinations. It should be noted that the psychiatric side effects are more common with higher doses of ketamine, especially when it is used for general anesthesia.[45] Benzodiazepines can ameliorate these side effects. Other adverse reactions to ketamine include laryngospasm, hypertension, and increased intracranial pressure.

Clinical trials report mixed results, with some demonstrating an improvement in airway pressures, gas exchange, and bronchospasm. Others have not been as supportive of using this agent in mechanically ventilated asthmatics. At this time, no large, randomized, prospective trials have been performed to support or discourage the use of ketamine in the setting of severe bronchospasm. As such, it should be considered a rescue agent to be used when conventional therapy (steroids, bronchodilators, appropriate ventilation settings, and adequate sedation) has proven ineffective.

The typical dosing for ketamine in status asthmaticus has not been clearly defined. Clinical trials have used an initial bolus anywhere from 0.1 mg/kg to 2.0 mg/kg, followed by infusions ranging from 0.15 mg/kg/hr to 2.5 mg/kg/hr for up to five days.[23] Because of the lack of clear evidence-based recommendations, it seems prudent to start with a lower bolus dose like 0.1 to 0.5 mg/kg, followed by an infusion starting at 0.15 to 0.25 mg/kg/hr. The infusion can be titrated upward until the desired clinical response of adequate sedation, improvement in gas exchange, and improvement in bronchospasm (as determined by chest auscultation and lower airway pressures) is attained. Furthermore, it makes sense to administer benzodiazepines when the ketamine is being weaned off to prevent emergence reactions.

Most of the time, the measures described above are sufficient to treat the patient with severe bronchospasm. Keep the vent rate low; administer albuterol, ipratropium, and prednisone; don’t stress about the $PaCO_2$; and let the patient get better. This usually works, until it doesn’t. When the patient is still deteriorating, the clinician should consider one or more rescue therapies. These include Heliox and therapeutic bronchoscopy. Inhalational anesthetics have been described in the literature, but the cumbersome nature of anesthesia machines and the potential toxicity of leaking anesthetic gases to hospital staff make this a less desirable option.

Heliox

Heliox refers to a blend of helium and oxygen, usually in a 70:30 ratio. A gas blender can be used to change this ratio to 60:40. When the fraction of oxygen exceeds 40%, the potential benefit of Heliox is lost. Therefore, Heliox should only be used when the patient can be adequately oxygenated with an FiO_2 of 40% or less.

The benefit of Heliox is with the helium having a much lower density than nitrogen gas. This translates into Heliox improving the tendency of inspired gas toward laminar flow, which improves gas flow through narrowed proximal and larger airways. More laminar and less turbulent gas flow in the conducting airways leads to better gas exchange and aerosol delivery of medications like albuterol to the respiratory and terminal bronchioles. This can also help reduce the work of breathing. Heliox can be delivered by facemask, through noninvasive positive pressure breathing, or via the mechanical ventilator.

Two issues must be addressed when using Heliox through the ventilator. The first is the mode of ventilation. Most newer ventilators are not calibrated for a mixture of helium and oxygen. The inspiratory valve may permit a larger volume of gas to be delivered than what is set in volume-control mode, and some ventilators will not register an accurate exhaled tidal volume. For this reason, pressure-control ventilation is preferable. The inspiratory pressure should be set at a level sufficient to attain rise of the chest and provide acceptable (if not normal) alveolar ventilation. In order to avoid barotrauma, keeping the inspiratory pressure less than 30 cm H_2O is advised, if possible. If volume-control ventilation is desired, then the clinician should either use a conversion table for the particular ventilator being used[46] to estimate the true tidal volume, or else periodically measure the exhaled tidal volume at the level of the endotracheal tube with a density-independent pneumotachograph.[47] Using pressure-control ventilation is easier.

The second issue is the FiO_2. Most ventilators have two gas inlets—one for 100% oxygen, and one for air (21% oxygen). The gas blender will mix the two to attain the FiO_2 selected on the ventilator. Administration of helium through the air inlet can result in a different FiO_2 actually delivered to the patient. In the case of pure helium going through the air inlet, the delivered FiO_2 may be less than what's selected (normally the air inlet has 21%

oxygen, and with pure helium there's 0% oxygen). More commonly, a premixed Heliox tank is connected to the air inlet. If the Heliox is, say, 70% helium and 30% oxygen, and the FiO_2 on the vent is set at 30% oxygen, then the patient will end up receiving a higher FiO_2 than the selected 30% (due to mixture of the gases). This may reduce the efficacy of the Heliox, especially if the true FiO_2 exceeds 40%. It can also increase the volume of gas delivered to the patient and increase the airway pressures. To make this even more complicated, different ventilators use different mixing valves and blenders. It's important to know how the particular ventilators you're using work with Heliox.

There are two ways around the issue of the FiO_2. The first is to directly sample the inspired gas with a density-independent measuring device, which is cumbersome. The second is to connect a premixed tank of Heliox to the air inlet of the ventilator and set the FiO_2 on the vent to 21%. This means that no supplemental oxygen is added to the Heliox mixture and that only the Heliox is delivered to the patient. The gas blender on the tank, or the mixture of the gas in the tank itself, can be used to control the "true" FiO_2— the vent may say the FiO_2 is 21%, but if the tank is full of 70:30 Heliox, then the patient is actually getting 30% oxygen. This is the easiest method, but it requires informing the nursing and respiratory staff that the FiO_2 is not actually 21% (despite what it says on the ventilator).

Therapeutic Bronchoscopy

Therapeutic bronchoscopy is occasionally necessary to clear the airways of thick mucus plugs and bronchial casts. Occlusion of large conducting airways can definitely affect lung mechanics and gas exchange and seems to limit the delivery of inhaled bronchodilators to smaller airways. One review of 93 cases of fatal asthma showed that airway obstruction by exudative secretions was a significant cause of death.[48] Early evaluation of the tracheobronchial tree with fiberoptic bronchoscopy should be considered in patients with severe bronchospasm, and mucus plugs should be aggressively lavaged. Giving mucolytics like N-acetylcysteine through the bronchoscope may be helpful, but this can cause bronchospasm. Instrumentation of the airways themselves with the bronchoscope can also cause immediate or

delayed bronchospasm. For “routine” cases of asthma, bronchoscopy is probably not warranted and may cause complications. For severe cases, however, the likelihood of significant mucus plugging or casting of the airways is higher and the benefits of bronchoalveolar lavage may outweigh the risk.

Wait It Out

One of the major challenges in the critical care of patients with severe bronchospasm is that they don’t get better right away. It may take several days or longer for the steroids and bronchodilators to take effect and for the inflammation and bronchospasm to subside. In the meantime, it is important to stay focused on the following goals:

- Maintain adequate (but not perfect) oxygenation—an SpO_2 88-95% is fine. Hyperoxia isn’t necessary or helpful.
- Reduce hyperinflation by giving the lungs plenty of time to exhale.
- Tolerate a respiratory acidosis, especially if “normalizing” the $PaCO_2$ and pH means injuring the lungs with high tidal volumes or dynamic hyperinflation. Prevention of ventilator-induced lung injury is far more important than a “good” ABG. Let the pH go down as low as 7.10 if necessary.
- Use therapies like Heliox, ketamine, and therapeutic bronchoscopy if necessary, but don’t let them distract you from the goals listed above.
- Provide good holistic critical care. That includes nutritional support, DVT prophylaxis, and mobilization when appropriate.
- Be patient. It takes time to get better. Put the patient on the right course, monitor for changes, and let your plan work. In an age of instant gratification, this can be the hardest part!

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* A drop in the systolic blood pressure by more than 10 mm Hg during inspiration. The “paradox” is that the heart is still beating, but the radial pulse may be absent. Pulsus paradoxus can also be seen with cardiac tamponade, constrictive pericarditis, anaphylaxis, pneumothorax, and other conditions.

* Alveolar flooding and collapse are usually not a problem with status asthmaticus or exacerbation of

COPD. Applying PEEP, especially with status asthmaticus, can worsen air trapping and hyperinflation. There is occasionally a role for applied PEEP with dynamic airway collapse, like in a COPD exacerbation, but to start with I recommend zero end-expiratory pressure (ZEEP).

Chapter 16

Prone Positioning and Neuromuscular Blockade

Two adjunctive strategies for treating severe ARDS that have been used for years are prone positioning and therapeutic neuromuscular blockade. These are often used in conjunction with each other, and the clinical rationale is improved ventilator-perfusion matching and alveolar recruitment. Until recently, neither treatment had shown an improvement in survival from severe respiratory failure (although there was proof of improved oxygenation).

In 2013, Guérin and colleagues published a multicenter randomized trial (PROSEVA) examining the effect of prone positioning for 16 hours, followed by 8 hours supine, in patients with ARDS.[49] They reported an overall reduction in mortality of 16.8%. In 2010, Papazian and colleagues published a multicenter, randomized, double-blind study (ACURASYS) that demonstrated a reduction in the hazard ratio for death from ARDS when a cisatracurium infusion was used for 48 hours early in the treatment of moderate-to-severe ARDS.[50] The publication of these two papers led to the inclusion of these therapies in professional guidelines and has prompted interest in these, and other, strategies for the treatment of ARDS.

Despite the enthusiasm that has greeted these findings, it's important to keep in mind that there are limitations with these and other studies, and that their findings should not result in wholesale application of prone positioning and neuromuscular blockade in every patient with ARDS. In this chapter, the pros and cons of each treatment will be discussed. If this seems like hedging, well, that's because it is. Both prone positioning and neuromuscular blockade have a place in the treatment of ARDS, and both have significant risks. Neither is a magic bullet, and neither is a substitute for lung-protective ventilation and good supportive critical care. By the time you're reading this,

there may be new developments either supporting or refuting (or both!) these therapies. For now, the focus should be on identifying the patients who may benefit while minimizing the risks.

In Favor of Prone Positioning

In ARDS, dorsal lung units tend to become more consolidated. Transpulmonary pressures are increased in dorsal alveoli and lower in ventral alveoli. At the same time, the gravitational effect on pulmonary blood flow leads to these units being relatively more perfused than the aerated ventral lung units. This has the effect of increasing the shunt fraction and worsening oxygenation. The rationale for prone positioning is that flipping the patient onto his abdomen will improve ventilation-perfusion matching and thereby improve gas exchange. At the same time, a more even distribution of aeration and transpulmonary pressure occurs. Prone position helps homogenize the pressure within the thorax, mitigating the effect of stress risers. This is the same thing that PEEP does, except that proning doesn't increase the force or mechanical power applied to the lungs.

There are other benefits as well. Prone positioning improves drainage of pulmonary secretions from the airways. Allowing the abdominal contents to be dependent (by padding the patient's chest and pelvis) reduces the pressure on the diaphragm and improves chest wall compliance. The weight of the heart, which is normally directed over the left lower lobe, is shifted centrally.

Previous studies of prone positioning were able to show improvement in pulmonary blood flow and oxygenation, but did not improve mortality.[51,52] This may have been due to using prone positioning in patients with less-severe ARDS, poorly defined protocols, and a shorter duration of the time spent prone. The 2013 Guérin study, on the other hand, was well-defined and included patients with a PaO_2/FiO_2 ratio $\leq$ 150. These patients were sufficiently ill enough to where a treatment benefit might become evident. This study also mandated that the time spent prone (16 hours at a time) was long enough for any physiologic benefit to occur. Earlier studies had prone times of 6-8 hours.

The risks of prone positioning include dislodgement of life support equipment like endotracheal tubes and vascular catheters; pressure injury to the eyes, face, and extremities; and the need for heavy sedation and often neuromuscular blockade. There is also risk of injury to unit staff, especially

when turning heavier patients. Many of these complications can be reduced or avoided by using a clearly defined protocol for turning and adequate staff training. While sedation and neuromuscular blockade have risks, limiting prone positioning to those patients who have moderate-to-severe ARDS (and stopping it once the patients begin to recover[*]) should keep the number of days spent heavily sedated to a minimum.

Arguments Against Prone Positioning

The centers that participated in the PROSEVA trial have ample experience with prone positioning for ARDS. The importance of staff education and protocols for proning cannot be overstated. The risks to both the patient and to the staff are highest during the turning process. Intensive care units that wish to make this a part of how they care for ARDS should develop checklists and practice doing it so that it can happen seamlessly when actually done for critically ill patients.

The PROSEVA trial did show a mortality benefit, but it's important to note that it was the first trial of prone positioning in ARDS to do so after numerous other clinical trials had failed. This may have been due to improvement in the process and a refinement of the indications and duration of treatment. It could also easily reflect the fact that clinical statistics are not exact and that occasionally a trial can demonstrate a benefit when none actually exists. The PROSEVA trial was very similar to another clinical study of prone positioning published in 2009.[53] That study looked at a similar number of patients (466, vs. 342 in PROSEVA) and included patients with a PaO_2/FiO_2 ratio ≤ 200. It also used a similar duration of proning (20 hours at a time in PS II vs. 16 hours in PROSEVA). There was the expected improvement in oxygenation, but no statistically significant difference in mortality. The fact that two very similar clinical trials reached very different conclusions suggests that a much larger tie-breaker trial is needed.

The final issue that clinicians should consider with PROSEVA is the overall reduction in mortality. There was a nearly 17% absolute risk reduction, which is **huge**. No other treatment in critical care medicine has been able to consistently reduce the risk of death that much. This may be a case of "if it looks too good to be true, it probably is." Hopefully, a large-scale trial of thousands of patients will be done in the future to settle the

issue.

In Favor of Therapeutic Neuromuscular Blockade

Much of the ventilator-induced lung injury seen in ARDS is due to high transpulmonary pressure in vulnerable alveoli and overdistension of relatively healthy lung units during mechanical ventilation. Therapeutic neuromuscular blockade, along with heavy sedation, aims to improve respiratory system compliance and patient-ventilator dyssynchrony. Inflammatory biomarkers in both the blood and in bronchoalveolar fluid are also reduced when neuromuscular blockade is used.[54] These effects putatively lower the risk of ventilator-induced lung injury and improve survival from ARDS.

The ACURASYS trial used a bolus of cisatracurium, followed by a continuous infusion, for 48 hours early in the treatment of moderate-to-severe ARDS ($PaO_2/FiO_2 \leq 150$). This led to an improvement in the hazard ratio of death at 90 days, along with a reduction in the incidence of pneumothorax (4% vs. 11.7%). The benefit was most pronounced in patients with a PaO_2/FiO_2 ratio ≤ 120, suggesting that neuromuscular blockade is most effective in the sickest patients. Other, smaller clinical trials have also suggested that a cisatracurium infusion may be beneficial.[31,55] Importantly, these trials did not show a higher risk of prolonged myopathy or ICU-acquired weakness when compared with the control groups.

Arguments Against Neuromuscular Blockade

The ACURASYS trial claimed a reduction in the 90-day hazard ratio of death, but the overall reduction in mortality was not statistically significant. In other words, patients who received cisatracurium lived longer than the control arm, but a similar number were dead by the 90-day mark. A reduction in the hazard ratio may be a meaningful outcome in a trial looking at a new treatment for, say, lung cancer—the five-year mortality may not be different, but the new drug may prolong life for another year or two. Most people would consider that successful. Most people would probably not consider an additional week or two of life in the ICU, intubated and attached to machines, to be a successful result.

There were also concerns regarding the external validity of the study. The rate of pneumothorax in the control group was nearly 12%, which seems higher than what's seen in clinical practice. This leads to questions regarding the ventilator strategy used, and it turns out that the prescribed tidal volume in this trial was 6-8 mL/kg PBW. This is a higher tidal volume than what's recommended for moderate-to-severe ARDS.

Nearly 22% of the control group in the ACURASYS trial received open label cisatracurium. This makes interpretation of the results difficult, as the study wasn't completely blinded. Patients with more pronounced dyssynchrony with the ventilator would be the ones expected to receive open-label neuromuscular blockade, and these would also be the ones in the control group. In an effort to preserve blinding, all patients in the study had to be sedated to the point of complete unresponsiveness prior to receiving either the cisatracurium infusion or placebo. Heavy sedation is also known to be associated with higher risks. These issues should not be discounted.

In 2019, the issue was reexamined in a larger trial of 1006 patients.[56] Similar inclusion criteria were used, and the ROSE study found no mortality benefit (or any other benefit, for that matter) with the use of cisatracurium in early ARDS.

Putting It Together

The point of the preceding arguments was not to convince you that all patients with ARDS should be proned and paralyzed, and it wasn't intended to say that proning and neuromuscular blockade are worthless. The truth is that both may have a role in moderate-to-severe ARDS ($PaO_2/FiO_2 \leq 150$), and they should be considered on a case-by-case basis. The patients most likely to benefit from prone positioning are those with significant dorsal consolidation as seen on CT imaging. Patients with more diffuse infiltrates may not see as much of a response to changes in respiratory mechanics and pulmonary blood flow. Additionally, the nursing care of other issues (long bone fractures, recent chest or abdominal surgery, brain injury, etc.) may be adversely affected with proning. Proper training and drilling of ICU staff, along with the use of a proning checklist, should minimize the risk of turning to both patients and caregivers.

At this time, there does not appear to be evidence for routine use of neuromuscular blockade in ARDS. That doesn't mean that it should never be

used, however. The patients most likely to benefit from therapeutic neuromuscular blockade include those with extremely poor respiratory compliance; those with significant dyssynchrony with the ventilator despite the best efforts of the clinician; and those with coexisting issues like abdominal compartment syndrome or intracranial hypertension where an improvement in thoracic compliance could lead to an overall improvement in hemodynamics and end-organ perfusion. Neuromuscular blockade should be questioned in patients receiving high-dose corticosteroids due to the higher risk of ICU-acquired weakness syndrome.

For this reason, as well, cisatracurium (a benzylisoquinolone that is metabolized in the plasma by Hofmann degradation) is preferred over aminosteroidal neuromuscular blockers like vecuronium or pancuronium—these agents have a higher risk of ICU-acquired weakness when concomitantly administered with steroids. They (the aminosteroidal drugs) also depend on hepatic and renal metabolism and their effects may be prolonged with hepatic or renal dysfunction, which are quite common in the ICU. Peripheral nerve stimulation should be used to monitor the depth of neuromuscular blockade, and a daily sedation/paralytic holiday should be considered.

Prone Positioning Checklist

Indications for Prone Positioning

Hypoxemic respiratory failure with the following features:

- PaO_2/FiO_2 ratio < 150 despite high PEEP or APRV
- Diffuse bilateral lung infiltrates
- Dorsal consolidation on CT (if available)

Contraindications for Prone Positioning

- **Prohibitive risk of pathogen exposure to ICU staff**
- Unstable cervical spine
- Significant long bone fractures
- Anatomical or treatment considerations that preclude proning

Minimum Necessary Personnel

- 1 respiratory therapist to control the airway and ventilator
- 4 turners (may be RN, MD, PCT, RRT, or student)
- 1 supervisor, who should not be involved in the proning process itself

Turning Process

A. PREPARE the patient

- Apply lubricant to eyes and tape eyelids closed
- Remove any jewelry from the patient's head or neck
- Remove any bite blocks
- Bolus necessary analgesia/sedation/neuromuscular blocker
- Confirm SpO_2 and $ETCO_2$ monitors are in place and functional

B. POSITION the personnel

- Two turners on either side of the patient (four total)
- Respiratory therapist at the head of the patient to manage the head, airway, and face pillow

- If available, one person to manage ventilator tubing and provide backup
- Supervisor at the foot of the bed

C. PAD the patient (if going from SUPINE to PRONE)

- Foam face pillow, making sure the endotracheal tube is not kinked (it may be necessary to cut out some of the foam padding)
- Two pillows each on the chest, lower pelvis, and shins
- Place a sheet over the patient (head to toe) and wrap snugly, bundling the pillows to the patient

D. DISCONNECT (if safe to do so for a brief time)

- Central lines (after necessary boluses)
- Arterial lines
- Hemodialysis lines
- Cardiac monitor leads

E. **TURN the patient—Supervisor should read each step aloud, with verbal confirmation by the team members**

1. Supervisor confirms that the airway and ventilator tubing are under control by the respiratory therapist.
2. Supervisor confirms that all lines and leads have been disconnected (SpO_2 and $ETCO_2$ monitors may be left in place, unless it interferes with the turning process).
3. On the supervisor's count, the team will turn the patient onto his left side, keeping the pillows tight against the body using the sheet.
4. Supervisor confirms that nothing needs to be repositioned.
5. On the supervisor's count, the team will turn the patient to the PRONE or SUPINE position, ensuring that the pillows and face pad are kept in the proper position.
6. Respiratory therapist confirms to the supervisor that the endotracheal tube is at the proper depth and that the tube is not obstructed, with an appropriate $ETCO_2$ waveform.
7. If PRONE, turners confirm to the supervisor that the patient is

appropriately padded, and that arms and legs are positioned comfortably.

8. If SUPINE, turners remove padding.
9. Reattach cardiac monitor leads, arterial line, and restart infusions.

Prone position should be maintained for 16 hours, followed by 8 hours in the supine position. Eye and mouth care is essential. Tube feeding in the prone position is permissible if the tube is post-pyloric; otherwise, hold tube feeding while prone and increase the rate of feeding while supine.

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* My practice is to keep the patient prone for 16 hours and then supine for 8 hours. This continues until the PaO2/FiO2 ratio is > 150 near the end of the 8-hour supine period.

Chapter 17

Airway Pressure Release Ventilation

Current understanding of lung-protective ventilation suggests that lower tidal volumes are better because they don't excessively distend the alveoli, and that a higher positive end-expiratory pressure (PEEP) is better because it keeps vulnerable alveoli from collapsing at the end of the respiratory cycle.[3,5] Prevention of the repetitive collapse and reopening of alveoli reduces the shear stress and "atelectrauma" seen with ventilator-associated lung injury.

High frequency oscillatory ventilation takes low tidal volume ventilation to the extreme, by using volumes less than anatomic dead space. Airway pressure release ventilation (APRV), on the other hand, works by taking the concept of higher PEEP and running with it.

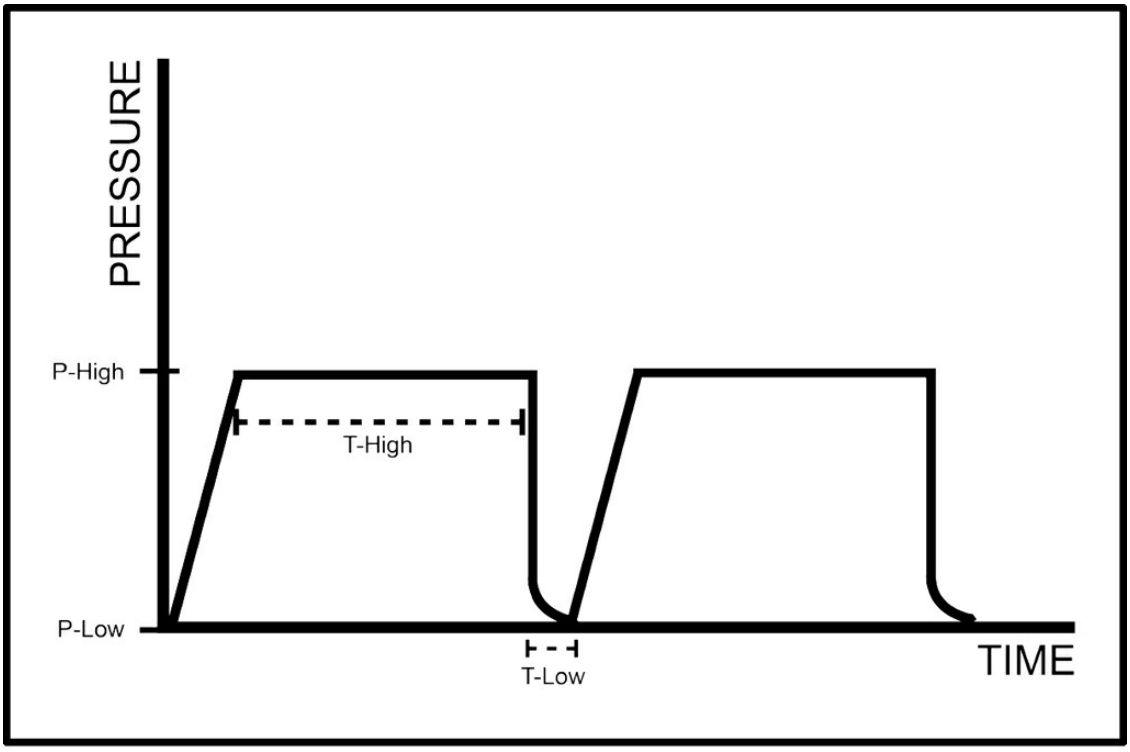
Severely ill or injured lungs, like those seen in ARDS, pulmonary contusions, and bilateral pneumonia, are characterized by a high shunt fraction. Flooded or collapsed alveoli are perfused, but gas can't make it to the alveolar-capillary membrane. Positive pressure ventilation can reduce this shunt fraction by recruiting, reopening, and stabilizing vulnerable alveoli.

If I took a patient with ARDS and put him on a CPAP of 35 cm H_2O and an FiO_2 of 100%, his oxygenation would improve. The continuous positive pressure would open up the alveoli, and oxygen would diffuse across the alveoli into the pulmonary capillaries. The problem, of course, would be ventilation. It's unlikely the patient could maintain his own minute ventilation, and without tidal breathing the $PaCO_2$ would rise drastically. Pushing more air in on top of a CPAP (or PEEP) of 35 would lead to very high distending pressures, even if the tidal volume were kept low.

What if, on the other hand, I didn't try to push more air in? Instead of giving a tidal volume, I can suddenly decompress the airways by lowering the pressure to zero. When that happens, air rushes out, carrying carbon dioxide with it. This would provide adequate ventilation. Of course, if I left the

pressure at zero for long enough, all of the vulnerable alveoli would collapse. This would increase the shunt fraction and reopening them could cause further lung injury. The answer, then, is to depressurize the airways long enough to let the gas escape but short enough to keep the alveoli from collapsing. This is what's happening during APRV.

The terminology for APRV may sound confusing, but it's really a simple system. Think of it as breathing on CPAP with intermittent releases. The CPAP is there to keep the lungs open and to maintain oxygenation. The releases periodically clear carbon dioxide from the lungs. As an added benefit, the patient can breathe spontaneously during APRV. This goes a long way toward improving VQ matching (via spontaneous diaphragmatic activity) and patient comfort, lessening the need for sedation.



APRV uses long periods of a high pressure with brief periods of a low pressure to improve alveolar recruitment and ventilation. Think of it like CPAP with intermittent releases.

APRV Terms and What They Mean

First of all, APRV™ is a proprietary term and is what this mode of ventilation is called on Dräger ventilators. It's called Bi-Vent™ on Servo ventilators, and BiLevel™ on Puritan Bennett. Some of the terms mentioned below may also have different names, depending on the brand of ventilator you're using. Despite the various names, it's all essentially the same stuff.

P_{HIGH}: the CPAP, so to speak. It's the pressure applied to the airways during the majority of the respiratory cycle, and it's the pressure needed to maintain open alveoli. A higher P_{HIGH} means a higher mean airway pressure and better oxygenation. As the patient's gas exchange and compliance improve, he'll need less of a P_{HIGH}.

T_{HIGH}: the time spent at the P_{HIGH}. It's the time between releases. A longer T_{HIGH} will increase the mean airway pressure (improving oxygenation), but it also means fewer releases per minute (which can raise the $PaCO_2$).

P_{LOW}: the pressure that the ventilator drops to during the releases. Generally, this is set at zero. The airways act like a natural flow resistor, so end-expiratory pressure rarely reaches zero, but having the P_{LOW} at zero creates the highest pressure gradient and facilitates better release of gas. If you need to raise the mean airway pressure, you can increase the P_{LOW}; however, recognize that this will limit ventilation.

T_{LOW}: the time spent at the P_{LOW}. It's short—usually between 0.4 and 0.8 seconds. This is enough time for the gas to escape, but short enough to keep most of the alveoli for collapsing. It can be extended if necessary to ventilate more CO_2, but this may lead to more derecruitment. Following the expiratory flow waveform is the best way to

adjust the T_{LOW}.

The mean airway pressure and the FiO_2 govern oxygenation in APRV. Because there are no distending tidal volumes, APRV lets you ventilate the patient with a higher mean airway pressure without excessively high peak airway pressures. Raising the P_{HIGH} or prolonging the T_{HIGH} increases the mean airway pressure. Raising the P_{LOW} is another option but is not as helpful.

Initial APRV Settings

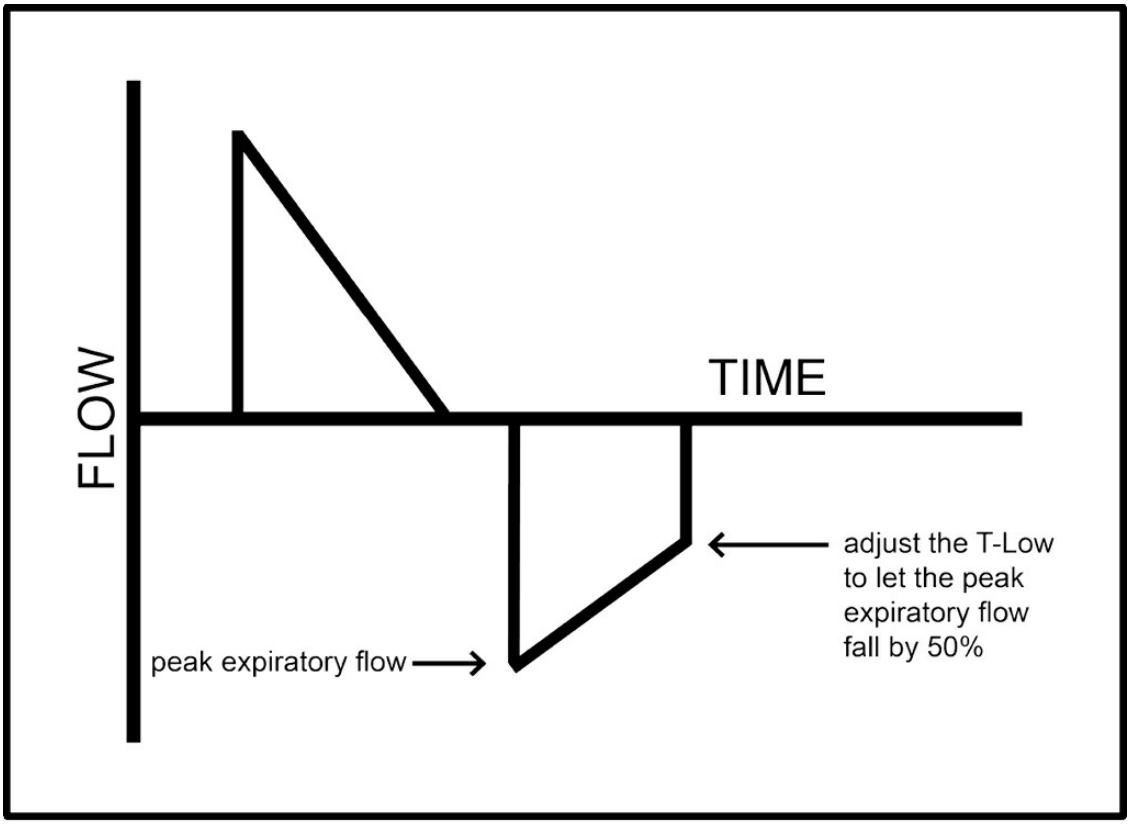
- FiO_2 100%
- P_{HIGH} 30-35 cm H_2O
- P_{LOW} 0 cm H_2O
- T_{HIGH} 4 seconds
- T_{LOW} 0.8 seconds, adjusted to let the peak expiratory flow drop by 25-50%

Ventilation is determined by the frequency of the releases, the time spent at T_{LOW}, and the gradient from P_{HIGH} to P_{LOW}. The number of releases per minute is mainly a factor of the T_{HIGH}—the longer the T_{HIGH}, the fewer the releases and vice versa. The more releases per minute, the lower the $PaCO_2$. Shortening the T_{HIGH} will blow off more CO_2, but it can also affect oxygenation by reducing the mean airway pressure.

The compliance of the patient's lungs determines how much gas will be released. If the compliance is, say, 20 mL/cm H_2O, then a drop from a P_{HIGH} of 30 to a P_{LOW} of zero will result in a release volume (similar to a tidal volume, in a way) of 600 mL. As the compliance improves, with either resolution of the lung injury or better recruitment of collapsed alveoli, the same pressure drop will have larger release volumes. This is one way to

know if the patient is getting better.

The time spent at T_{LOW} is also important. The longer the time, the more gas can escape (and the lower the $PaCO_2$). However, this will lead to more alveolar derecruitment. The best way to adjust the $PaCO_2$ is to look at the expiratory flow waveform on the vent. The expiratory flow rate should drop by around 25-50%, and then the ventilator should repressurize to the P_{HIGH}. This seems to be the sweet spot for allowing ventilation while maintaining recruitment. Patients with COPD may need a slightly longer T_{LOW}, letting the expiratory flow fall by 75%; patients with poorly compliant lungs might need a shorter T_{LOW} (fall in expiratory flow of only 25%) to maintain recruitment. For the most part, keeping the drop in flow around 50% is a good starting point. Don’t let the expiratory flow return to baseline—that’s too much time and you’ll allow a lot of alveoli to collapse.



If oxygenation is the biggest problem, the T_{LOW} can be shortened to allow a drop in expiratory flow of 25%. This will result in less CO_2 being ventilated but will also keep some additional alveoli open and improve oxygenation.

If ventilation is the more concerning issue, the T_{LOW} can be lengthened to allow a drop in expiratory flow of 75%. This will allow more CO_2 to be ventilated but may result in more alveolar derecruitment, which could affect oxygenation.

Weaning APRV

Weaning on APRV is easy. Keep in mind that this is nothing more than glorified CPAP. The patient can breathe on his own at the P_{HIGH}, and even if the tidal volumes are small, it's contributing to ventilation and to VQ matching. As the patient's compliance and gas exchange improve, he'll need less of a P_{HIGH} and fewer releases a minute. This is what's called the "drop and spread" method of weaning—the P_{HIGH} is lowered in 1-2 cm increments,

and the T_{HIGH} is gradually extended.

Once the T_{HIGH} is 8-10 seconds and the P_{HIGH} is less than 15, the patient can be switched to pressure support ventilation. Adding a small amount of PS (5-10 cm) makes up for taking away the intermittent releases. A typical switch would be if a patient were on APRV with a P_{HIGH} of 15 and a T_{HIGH} of 10 sec, and you changed the vent to pressure support ventilation with a CPAP of 12 (just under the P_{HIGH}) and a PS of 8 (to boost his spontaneous breathing). Once he's on PSV, you can lower the CPAP as the oxygenation improves and adjust the PS to maintain comfortable spontaneous breathing.

As an aside, I don't recommend using PS at a P_{HIGH} more than 20, even though it's an option on some vents—it can increase the transpulmonary pressure during spontaneous breathing and lead to lung injury.[57]

Limitations of APRV

Use of a prolonged high inspiratory pressure may have a predictably negative effect on hemodynamics, particularly if the patient is suffering from hypovolemia or right ventricular dysfunction. Air-trapping is also an issue—APRV generally creates some autoPEEP, which is not a problem with ARDS. In patients with asthma or COPD, however, this can become a significant issue and APRV might not be the mode of choice.

Keep in mind that when restrictive lung physiology meets obstructive, restrictive wins. In practical terms, that means that a patient with COPD who is in an automobile crash and has pulmonary contusions will act more like ARDS, at least at first. In this situation, APRV is fine so long as attention is paid to the T_{LOW}. As the pulmonary contusions heal, however, the airway obstruction from COPD will become more prominent and it will take a progressively longer T_{LOW} to get the desired drop in expiratory flow. You can either prolong the T_{LOW} to get the expiratory flow to drop by 50-75%[*], or you can switch to volume assist-control and set the ventilator to permit adequate time for exhalation.

Only a few clinical trials comparing APRV to conventional low tidal volume ventilation have been done. One review suggested that early application of APRV was associated with lower mortality and a lower incidence of ARDS in trauma patients, but the overall incidence of ARDS

was low, and this was a retrospective review.[58] Another meta-analysis of six RCTs examining APRV suggested a mortality benefit, but there were only 375 patients total among the six trials included in the analysis.[59] The largest randomized controlled trial of APRV and conventional ventilation to date in adults studied 138 patients,[60] and the largest trial in pediatrics studied 152 patients.[61] Both of these trials demonstrated improvement in oxygenation but did not have a statistically significant mortality benefit. Clearly, a larger trial is necessary; for now, however, APRV is a potentially beneficial ventilator strategy for moderate to severe ARDS.

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* This can require a T_{LOW} of 2-3 seconds, or sometimes even longer. That may confuse unit staff who are used to seeing a short T_{LOW} in the 0.5-0.8 second range. Emphasize that it's the drop in the expiratory flow that matters, not the time itself.

Chapter 18
Inhaled Pulmonary Vasodilators

Positive airway pressure has a beneficial effect on left ventricular function by reducing both preload and afterload (the transmural pressure across the left ventricle). At the same time, however, positive airway pressure can worsen right ventricular function—the normally low-pressure pulmonary vascular circuit now is subjected to significant pressure from the ventilator. Hypoxic pulmonary vasoconstriction also increases the workload on the right ventricle. Most of the time, this doesn't affect hemodynamics too much, and fluid loading is sufficient to maintain right ventricular output. In some patients, though, pulmonary hypertension and right ventricular dysfunction can have a notably adverse effect on both cardiac and pulmonary function.

Right ventricular (RV) dysfunction and even overt RV failure can be seen with severe ARDS. It is also seen with massive or submassive pulmonary embolism, right ventricular infarction, and in patients with preexisting pulmonary hypertension (chronic obstructive pulmonary disease, obstructive sleep apnea, connective tissue diseases, primary pulmonary hypertension, etc.). RV failure can be particularly difficult to treat—the right ventricle is normally a thin-walled structure that operates best in conditions of low vascular pressure and resistance. A sudden increase in pulmonary vascular resistance is hard for the RV to deal with—it just doesn't have the muscle mass of the left ventricle. Inotropes like milrinone and dobutamine can be used to "whip the heart," but an increase in cardiac output is often neutralized by a corresponding rise in myocardial oxygen consumption. In this situation, a selective pulmonary arterial vasodilator may prove to be helpful.

The most commonly used pulmonary arterial dilator in critical care medicine is inhaled nitric oxide (iNO). iNO can be delivered by mask or through the endotracheal tube and has a rapid vasodilatory effect on pulmonary arterioles and capillaries. One particular advantage of iNO is that it will only cause vasodilation in the alveolar-capillary beds that it reaches.

This has the effect of improving ventilation-perfusion matching in patients with severe hypoxemia. Inhaled prostacyclin can also be used and has the same physiologic effect. Intravenous pulmonary vasodilators like prostacyclin and alprostadil can be used but tend to have a much more potent effect on hemodynamic function and often cause hypotension.

There have not been many clinical trials of inhaled prostacyclin, and the evidence base is limited. iNO has been studied much more extensively, and so further discussion will center on the use of iNO. This does not mean that inhaled prostacyclin is not effective, and it may work just as well as iNO in similar clinical settings. It is important to note that neither iNO nor inhaled prostacyclin are FDA-approved for use in adults with ARDS or right ventricular failure, and any use is off-label.

The allure of inhaled pulmonary vasodilators is that they cause selective vasodilation only in the lung units that they can reach; they have a rapid onset and offset; that they have minimal adverse hemodynamic effects; and that there are no downstream metabolites. For years, this was thought to be the case. iNO was believed to be inactivated immediately by reacting with hemoglobin in the pulmonary capillaries. Recent research has shown that this is not the case. iNO reacts with hemoglobin and leads to formation of nitrite and S-nitrosohemoglobin. Nitrite can be recycled in downstream tissues to nitric oxide, which can cause systemic capillary vasodilation. S-nitrosohemoglobin also induces nitric oxide production, particularly in the setting of tissue hypoxia. This couples vasodilation and deoxygenation, which may lead to mitochondrial dysfunction. This has been demonstrated in clinical trials, where use of iNO is associated with a higher rate of renal failure.[62] Presumably, the toxic effects of these metabolites are not limited to the kidneys, which means that the metabolites of iNO could contribute to multisystem organ dysfunction.

iNO and ARDS

In patients with ARDS, iNO may improve oxygenation via selective pulmonary vasodilatation. No studies have shown a survival benefit with this therapy, however, and a recent meta-analysis[63] of nine clinical trials concluded that, “Nitric oxide does not reduce mortality in adults or children with acute respiratory distress syndrome, regardless of the degree of hypoxemia.” The reason for the lack of benefit seems to be in line with other

therapies that have been shown to improve oxygenation but not survival—very few patients with ARDS die of refractory hypoxemia. The majority die of multisystem organ failure, and the potentially toxic metabolites of iNO may potentiate this. Therefore, iNO should only be used in ARDS as a true rescue therapy. It may be helpful in patients with a PaO_2/FiO_2 ratio less than 55 despite optimal care and who are not candidates for other rescue therapies that have been proven to be beneficial (prone positioning, veno-venous ECMO).

iNO and Right Ventricular Failure

Acute right ventricular failure is primarily treated with fluid loading and inotropic support. Dobutamine and milrinone are inotropes that increase right ventricular contractility. Milrinone, a phosphodiesterase-III inhibitor, also has vasodilatory properties on the pulmonary circulation. Levosimendan is another calcium-sensitizing inodilator, but it is not commercially available in the United States.

RV failure is often associated with moderate-to-severe hypoxemia and pulmonary dysfunction. Conventional ventilator strategies that use high levels of PEEP or increase the mean airway pressure (like APRV) can worsen right ventricular function and increase pulmonary vascular pressures. Inhaled nitric oxide or prostacyclin can be used to lower the pulmonary vascular resistance, thereby improving right ventricular function and improving gas exchange.

When initiating inhaled pulmonary vasodilators for right ventricular failure, a pulmonary artery catheter or a central venous pressure monitor is strongly encouraged. Echocardiography can also be used to evaluate contractility and to measure pulmonary artery pressure, but it isn’t available continuously and is not ideal for titrating medications. The pulmonary artery catheter can continuously measure pulmonary artery pressure, cardiac output, and SvO_2. It can also be used to calculate the pulmonary vascular resistance. This is very useful for differentiating between conditions that cause pulmonary arterial hypertension and those associated with pulmonary venous hypertension. Selective pulmonary vasodilators tend to be more effective for the former.

Pulmonary vascular resistance (PVR) can be calculated by measuring the

mean pulmonary artery pressure and the pulmonary artery occlusion pressure at end-expiration. The difference between the two measurements is then divided by the cardiac output (in L/min).

$$\text{PVR} = [\text{mean PAP} - \text{PAOP}] / [\text{CO}]$$

A patient with a normal mean pulmonary artery pressure (20 mm Hg), pulmonary artery occlusion pressure (10 mm Hg), and cardiac output (5 L/min) would have a pulmonary vascular resistance of 2 mm Hg-min/L, or Wood units. Normal PVR is 2-3 Wood units.* Conditions that elevate both the mean PAP and the PAOP (most commonly left ventricular dysfunction, but also mitral and aortic valvular disease) are characterized by pulmonary hypertension and a normal PVR. This is often referred to as pulmonary venous hypertension. The high pressure in the left atrium leads to high right-sided pressures in order to keep the blood flowing. Caution should be used with any kind of pulmonary vasodilator—lowering the mean PAP, while the PAOP remains elevated, often leads to pulmonary edema.

Consider a patient who has severe systolic CHF. He has a mean PAP of 40 mm Hg and a PAOP of 30 mm Hg. The PAOP (a.k.a. the wedge pressure) represents left atrial pressure. Left atrial pressure equals left ventricular pressure at the end of diastole, when blood stops flowing from the atrium to the ventricle. The left ventricular end-diastolic pressure is elevated due to severe CHF. The only way that blood can flow from the right ventricle through the pulmonary vasculature and into the left ventricle is if the pulmonary artery pressure is higher than the left ventricular pressure. Now, this patient is started on iNO. The mean PAP falls, as predicted. iNO is a selective pulmonary vasodilator, which means that it will not reduce the left ventricular afterload. The left atrial pressure remains the same. If the mean PAP is now 28, and the left atrial pressure is 30, you can see where this is going. Blood flow will reverse, leading to pulmonary edema and hypotension.

Pulmonary arterial hypertension, on the other hand, is characterized by an imbalance between the mean PAP and the PAOP. Thromboembolic disease, connective tissue disease, and chronic hypoxemia are common causes. A patient with a mean PAP of 45 mm Hg, PAOP of 15 mm Hg, and a cardiac output of 6 L/min has PVR of 5 Wood units, suggesting pulmonary arterial

hypertension. Right ventricular dysfunction with a PVR ≥ 4 Wood units may improve with a pulmonary vasodilator.

It is important to remember that inhaled nitric oxide or prostacyclin is an adjunctive therapy, and not a treatment in itself. The underlying condition leading to right ventricular failure should be treated aggressively. Pulmonary embolism should be treated with anticoagulation and thrombolysis. Acute chest syndrome in patients with sickle cell disease should be treated with antibiotics and exchange transfusion. Acute myocardial infarction should be treated with reperfusion therapy. Attention to volume status is crucial—while hypovolemia will certainly lead to hypotension, volume overload will cause bowing of the interventricular septum and compromise left ventricular filling. Euvolemia, guided by echocardiography and/or pulmonary artery catheter monitoring, should be achieved by diuresis or renal replacement therapy.

Administration of iNO and Inhaled Prostacyclin

iNO is available with a commercial delivery system that has a long track record of reliability and safety. Using an unapproved, self-made delivery system has the risk of unreliable dosing of iNO and potentially toxic exposure of the patient and staff to nitrogen dioxide. Use the commercial system!

Inhaled prostacyclin can be reconstituted in saline and delivered by a jet nebulizer system modified for use with mechanical ventilation. This requires an aerosol delivery device that can be coordinated with the ventilator's inspiratory cycle, which has been described in the literature.[64]

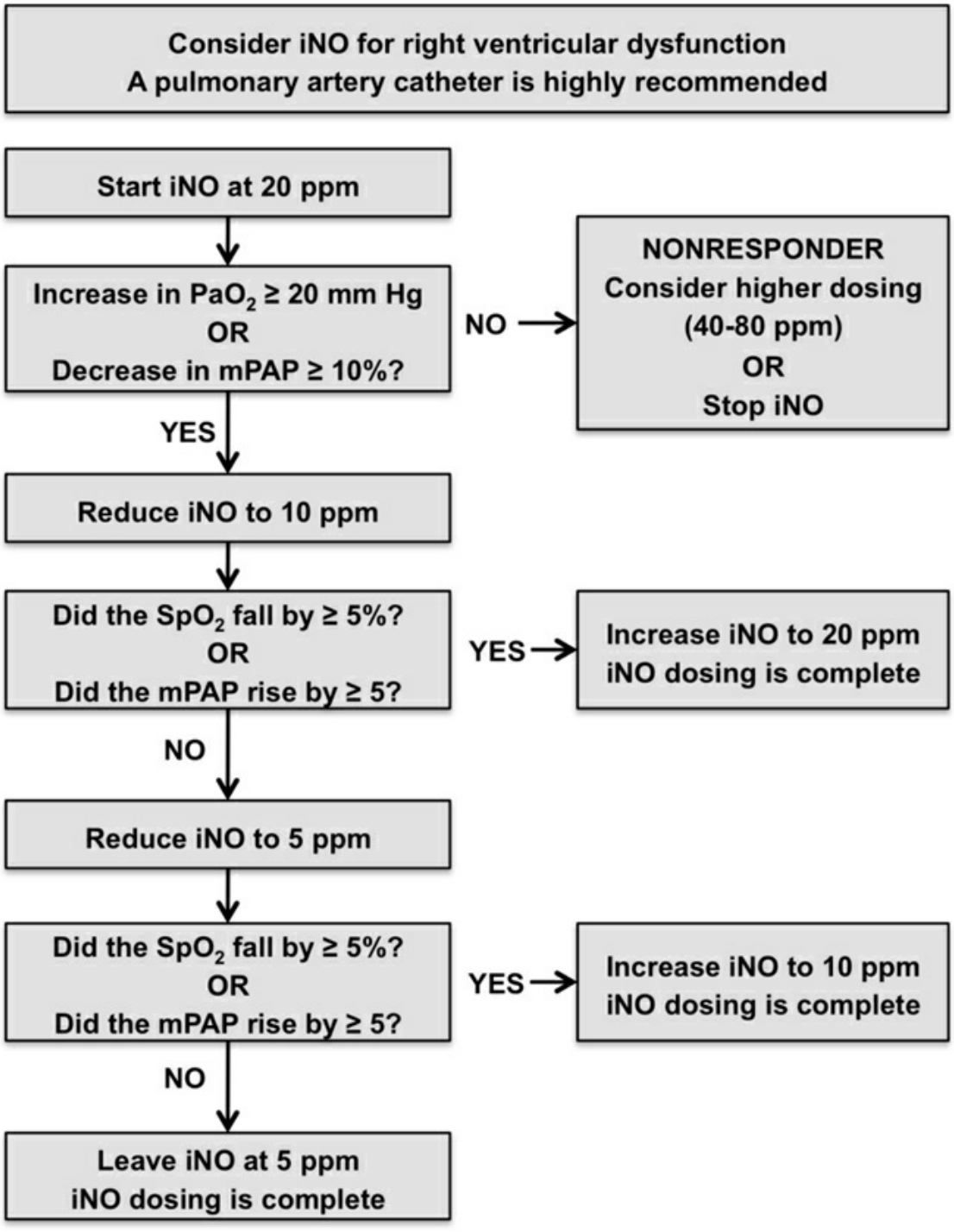
Initial Dosing of iNO

iNO should be started at 20 parts per million (ppm). A successful response is a reduction in the mean pulmonary artery pressure by at least 10%, and usually an improvement in the PaO^2 by at least 20 mm Hg. If the patient does not respond within 5-10 minutes, then a higher concentration (40 ppm, or even 80 ppm) can be tried. Most patients who are going to respond will do so at 20 ppm. iNO should be stopped in those patients who do not have an initial response to therapy.

In patients who respond, the dose of iNO should be lowered in 5-10 ppm

increments every 15-30 minutes, to a floor of 5 ppm. An increase in the mean PAP by ≥ 5 mm Hg, or a fall in the SpO_2 by ≥ 5%, should be treated by increasing the dose of iNO back to the level where it was effective.

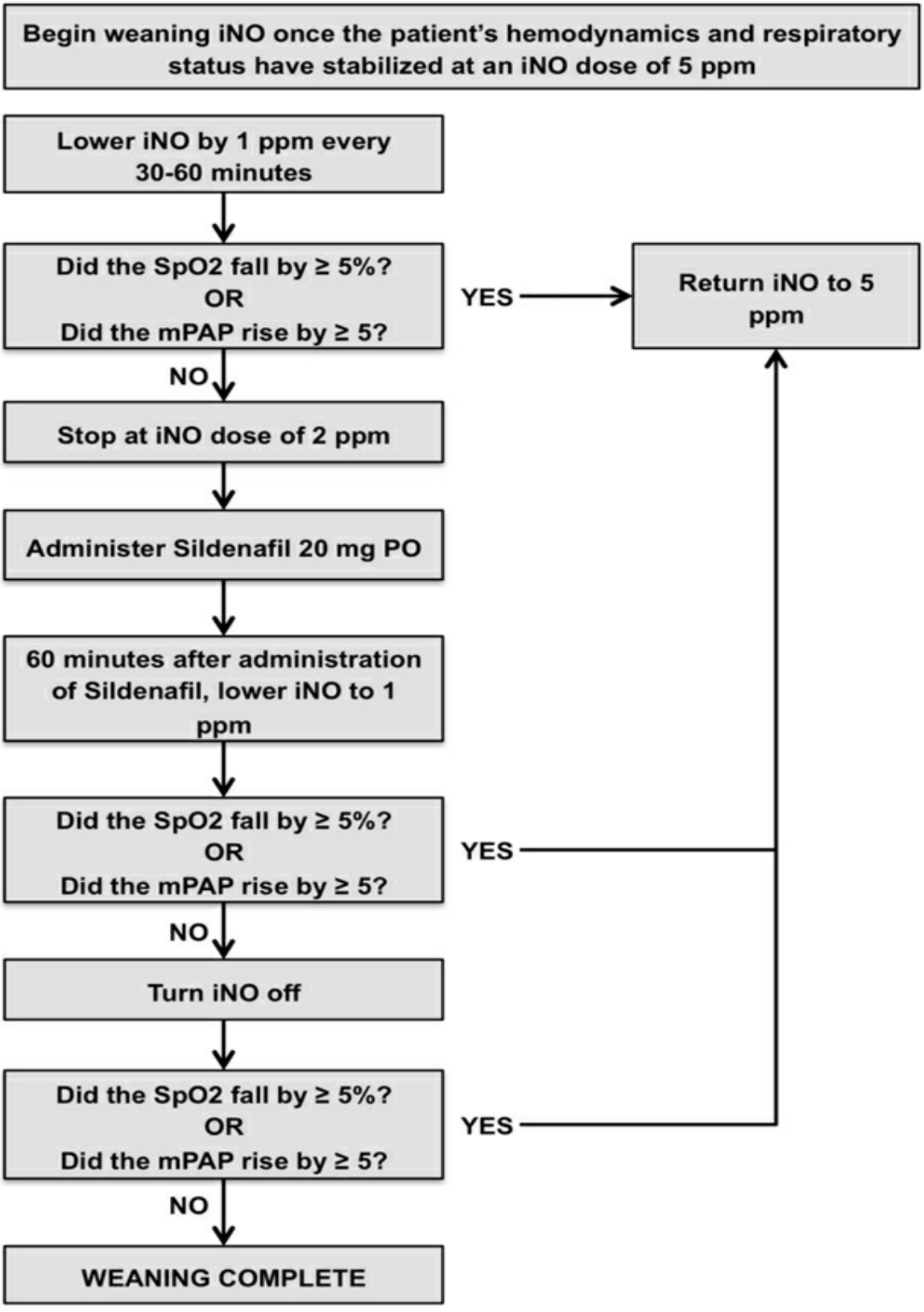
iNO Initial Dosing Algorithm



Weaning iNO

Once the patient has begun showing signs of recovery (improvement in gas exchange, less need for inotropes), iNO can be reduced or stopped altogether. This should be done slowly, as abrupt discontinuation of the drug can lead to rebound hypoxemia and pulmonary hypertension.

When the patient is tolerating an iNO dose of 5 ppm, the drug can be weaned off. The iNO dose should be lowered by 1 ppm every 30 minutes. If the mean PAP increases by ≥ 5 mm Hg, or the SpO_2 falls by ≥ 5%, the iNO should be returned to 5 ppm and further attempts at weaning should be postponed for at least 12 hours. Once the iNO is at 2 ppm, a single dose of sildenafil 20 mg can be given (if it's not already being administered). This may help prevent rebound pulmonary hypertension as the drug is weaned off. After administration of the sildenafil, continue to reduce the iNO by 1 ppm every 30 minutes until it's off.


Begin weaning iNO once the patient's hemodynamics and respiratory status have stabilized at an iNO dose of 5 ppm
Lower iNO by 1 ppm every 30-60 minutes
Did the SpO2 fall by ≥ 5%? OR Did the mPAP rise by ≥ 5?
YES
Return iNO to 5 ppm
NO
Stop at iNO dose of 2 ppm
Administer Sildenafil 20 mg PO
60 minutes after administration of Sildenafil, lower iNO to 1 ppm
Did the SpO2 fall by ≥ 5%? OR Did the mPAP rise by ≥ 5?
YES
NO
Turn iNO off
Did the SpO2 fall by ≥ 5%? OR Did the mPAP rise by ≥ 5?
YES
NO
WEANING COMPLETE

* PVR is often expressed in dyne-sec-cm-5. This is obtained by multiplying the number of Wood units by 79.9. I'm not sure why this is. I find it easier to use Wood units.

Chapter 19

High Frequency Oscillatory Ventilation

Numerous studies have shown the benefit of low tidal volume ventilation in ARDS. The primary determinant of ventilator-induced lung injury seems to be volutrauma, so it makes sense to keep the tidal volume as low as possible while maintaining adequate gas exchange. High frequency oscillatory ventilation (HFOV) aims to do this using ultra-fast tidal volumes that are less than the patient's anatomic dead space.

Watch a dog pant—he's not pulling in very much tidal volume, but somehow, he's still alive. This is basically the premise behind HFOV. A mechanical diaphragm oscillates between 3 and 15 times a second. This creates a "push-pull" action on the column of air extending from the endotracheal tube all the way to the alveoli.

Mechanisms of Gas Exchange in HFOV [65]

Direct convective gas flow: some alveolar beds are close enough to the large airways that oxygen-rich gas is carried into them, and carbon dioxide-rich gas is ventilated away. This makes up a small portion of total gas exchange in HFOV but is the primary mechanism of gas exchange in conventional ventilation.

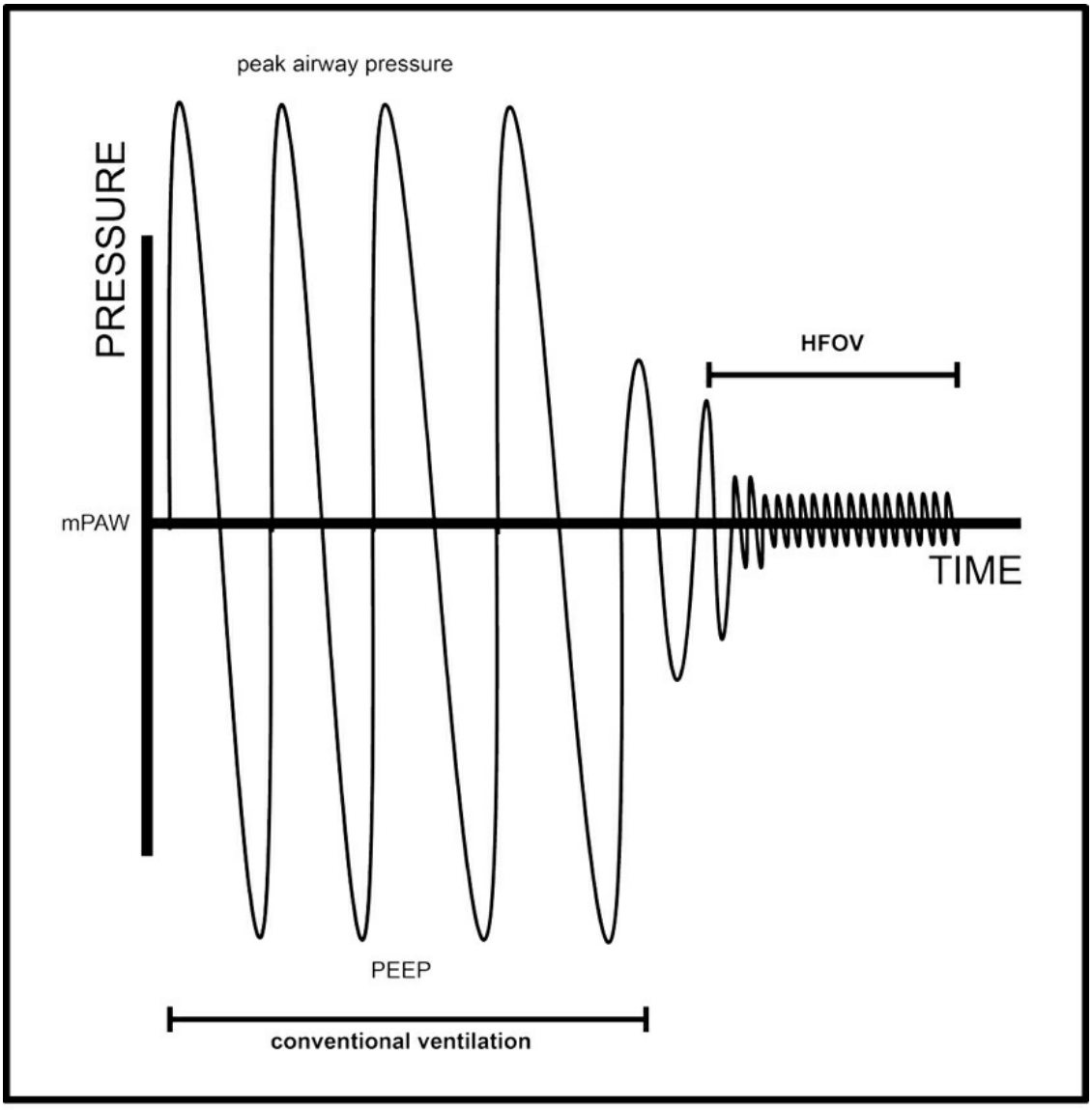
Taylor Dispersion: the theory behind this is that the inspired gas is pushed down the center of the column by the oscillatory pressure, while the gas from the alveoli remains

along the outer edge of the column and is gradually pushed out. Conceptually, think of a piston being pushed slowly down a slightly larger cylinder of liquid. As the piston gets closer to the bottom of the cylinder, the liquid is forced out around the edges.

Molecular Diffusion: at the level of the respiratory and terminal bronchioles, oxygen and carbon dioxide are agitated by the turbulent gas flow created by oscillation. This results in diffusion of oxygen into the alveoli, to be taken up by the capillaries.

Pendeluft: this describes the to-and-fro motion of gas from one alveolar bed to another. Gas from alveoli that are better ventilated will travel into alveoli that are less ventilated, thereby improving gas exchange. This happens via respiratory bronchioles and collateral channels between alveoli.

HFOV may be useful as a rescue mode of ventilation for severe hypoxemic respiratory failure, such as ARDS. It's also a useful mode when a patient has a large bronchopleural fistula and is losing a significant part of the tidal volume via a chest tube. The attraction is being able to increase the mean airway pressure, and thereby oxygenation, without exposing the lungs to high distending pressures and volumes (which we know are bad). HFOV has its own terminology, which is very different from conventional ventilation.



HFOV maintains a near-constant mean airway pressure (mP_{AW}) without the large swings in pressure seen with conventional ventilation. The oscillations are measured in frequency per second (Hz), not breaths per minute.

Oxygenation in HFOV is affected by the FiO_2 and the mean airway pressure (mP_{AW}). Recruitment maneuvers can also be done by raising the mP_{AW} and stopping the oscillations—this is essentially the same as using high-level CPAP to open up collapsed alveoli.

Ventilation is controlled by the frequency of the oscillations (*f*) and the

amplitude. The *f* is measured in Hertz, or oscillations per second. Thus, an *f* of 3Hz means the mechanical diaphragm is oscillating three times a second, or 180 times a minute. Here's an important point—the higher the frequency, the less convective gas flow (and more gas dispersion). This means that the tidal volume is reduced with faster oscillations. Raising the frequency (e.g., from 5Hz to 10Hz) will lower the tidal volume and lead to a rise in $PaCO_2$. Lowering the frequency will lower the $PaCO_2$. The frequency range on the oscillating ventilator is 3Hz to 15Hz.

Amplitude refers to the change in pressure across the oscillating diaphragm, and ranges from 8 to 90 cm H_2O. While this pressure can be quite high, it's important to remember that the pressure differential will dissipate as it travels down the ventilator circuit and the large airways. At the alveolar level, this pressure change is barely noticeable. Increasing the amplitude will increase the force of oscillation and improve gas mixing. Increasing the amplitude will lower the $PaCO_2$, while lowering it can lead to an increase in $PaCO_2$. Generally, the amplitude is set to a level that makes the patient's thighs jiggle (scientific, I know), and ventilation is controlled by changes in the frequency.

If the $PaCO_2$ remains unacceptably high, two other changes can be made to the ventilator. Remember that Taylor dispersion is like a piston being pushed into a larger cylinder—oxygen-rich gas is in center of the gas column, being pushed slowly into the alveoli, while CO_2-rich gas is on the periphery and is gradually forced out. When the gas flow stops momentarily, gas molecules diffuse evenly in the column. In HFOV, the gas "piston" travels down the column during the inspiratory time, or T_I. The T_I is usually set to take up 33% of the oscillatory cycle. By increasing the T_I to 50%, we can push the piston more and keep the CO_2 on the outside of the column from mixing with the delivered oxygen. This will improve CO_2 excretion.

Likewise, we can make the column a little wider to force out more of the CO_2. Normally, exhaled gas escapes through the endotracheal tube. To allow more CO_2-rich gas to be cleared, we can create a leak around the tube's cuff. This is referred to as a 5 cm cuff leak. To do this, deflate the cuff until the mP_{AW} drops by 5 cm H_2O. Then, increase the bias flow (inspired gas flow) until the mP_{AW} returns to its original level.

Initial HFOV Settings [66]

- Set the FiO_2 at 100%
- Set the m_{PAW} at 45 cm H_2O and hold at this level for 45 seconds (recruitment maneuver)
- After the recruitment maneuver, set the m_{PAW} at 35 cm H_2O
- Amplitude of 80, adjusted to see jiggling thighs
- Frequency of 5Hz
- • T_I 33%

Adjustments to HFOV can be made as described above. In severe respiratory failure, where you are likely to be using HFOV, you need to remember that having a perfect-looking ABG is not necessary or even desirable. Use the lowest FiO_2 needed to keep the PaO_2 55-70 and tolerate hypercapnia as long as the pH is in the 7.20 – 7.35 range.

As oxygenation improves, wean the FiO_2 and the mP_{AW}. Once the patient can maintain acceptable gas exchange with a mP_{AW} of 24 and an FiO_2 of 50%, it's time to consider switching back to conventional ventilation.

Limitations of HFOV

So, what's the downside to HFOV? As it turns out, there are several. First, there's only one commercially available ventilator in the U.S. that can provide HFOV for adults, at least at the time of this writing—the Sensormedics 3100B (Viasys® Healthcare, Yorba Linda, CA). This vent can't do anything else, so switching from conventional ventilation to HFOV, or vice versa, requires a ventilator change. Second, there are no alarms on the ventilator to tell you that there's something wrong with the patient. There is no high-pressure alarm or low tidal volume alarm or apnea alarm. This means that clinical examination needs to be very thorough, and you will end up ordering a lot of ABGs and chest X-rays. Third, it's difficult to clear

secretions without convective gas flow. Mucus plugging is a common problem with the oscillator. Fourth, HFOV is not exactly a comfortable mode for the patient. He can't breathe spontaneously, and he may not like all that jiggling. As such, heavy sedation and sometimes even neuromuscular blockade are necessary.

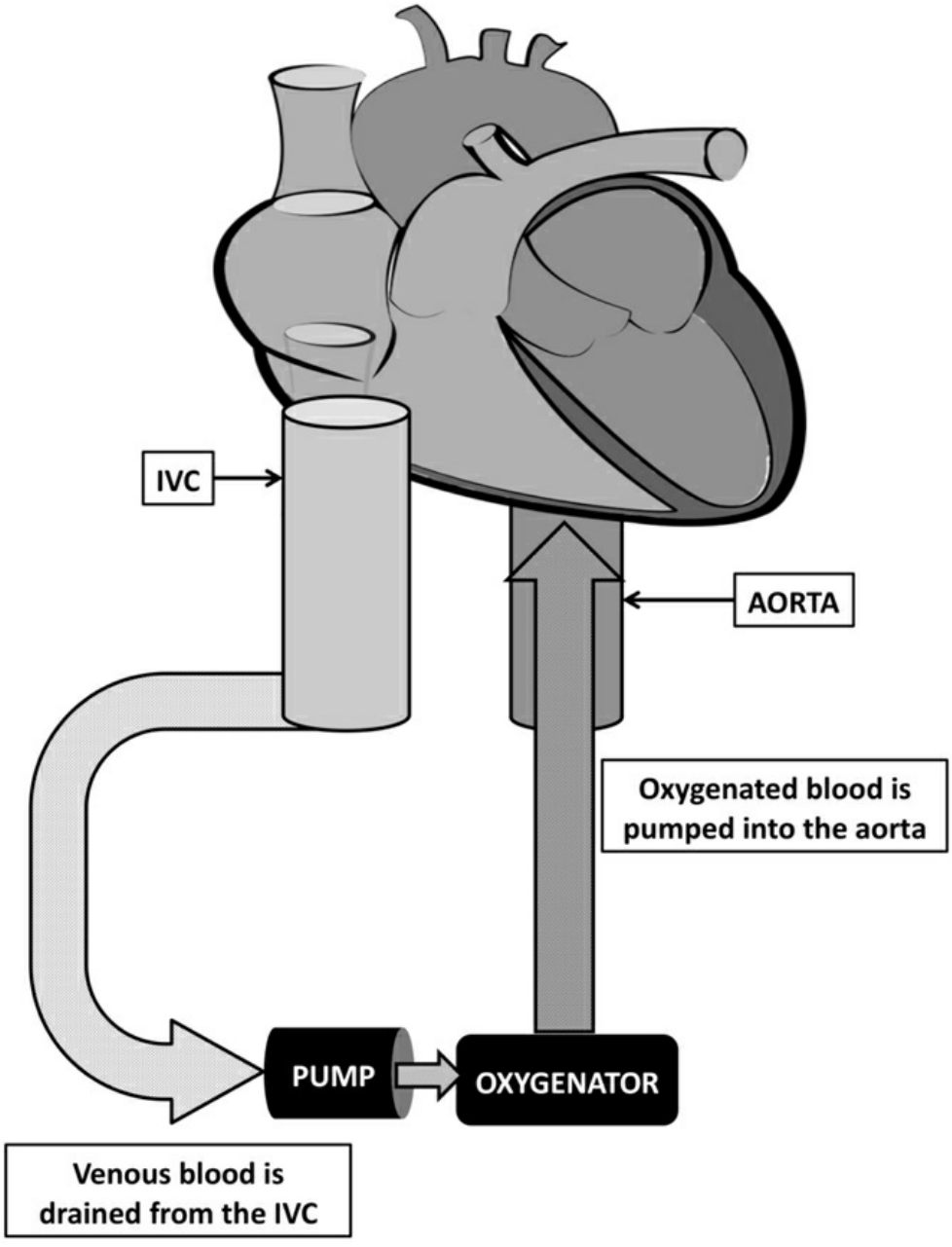
Fifth, and most importantly, current medical evidence doesn't support the routine use of HFOV. The OSCILLATE trial, published in 2013, was a multicenter trial examining the use of HFOV early in the treatment of moderate-to-severe ARDS.[67] The investigators found no evidence of benefit and a trend toward increased in-hospital mortality. This was validated by the OSCAR trial, another multicenter trial of HFOV in ARDS that found similar results.[68] For this reason, HFOV should be limited to those patients who have a specific need like a large bronchopleural fistula, or those with truly refractory hypoxemia ($PaO_2/FiO_2 < 55$) when other rescue therapies have either failed or are not an option.

Chapter 20
Veno-Venous ECMO

There are times when a patient's lung disease is so severe that adequate gas exchange is either impossible or can only be accomplished with prohibitively high airway pressures and tidal volumes. When this is the case, veno-venous extracorporeal membrane oxygenation (VV ECMO) should be considered as a rescue therapy. This chapter is simply an overview of the use of extracorporeal support and is designed to familiarize the reader with the rationale for its use. Those desiring to treat patients with ECMO are strongly encouraged to attend a training program sponsored by the Extracorporeal Life Support Organization (ELSO).

VV vs. VA

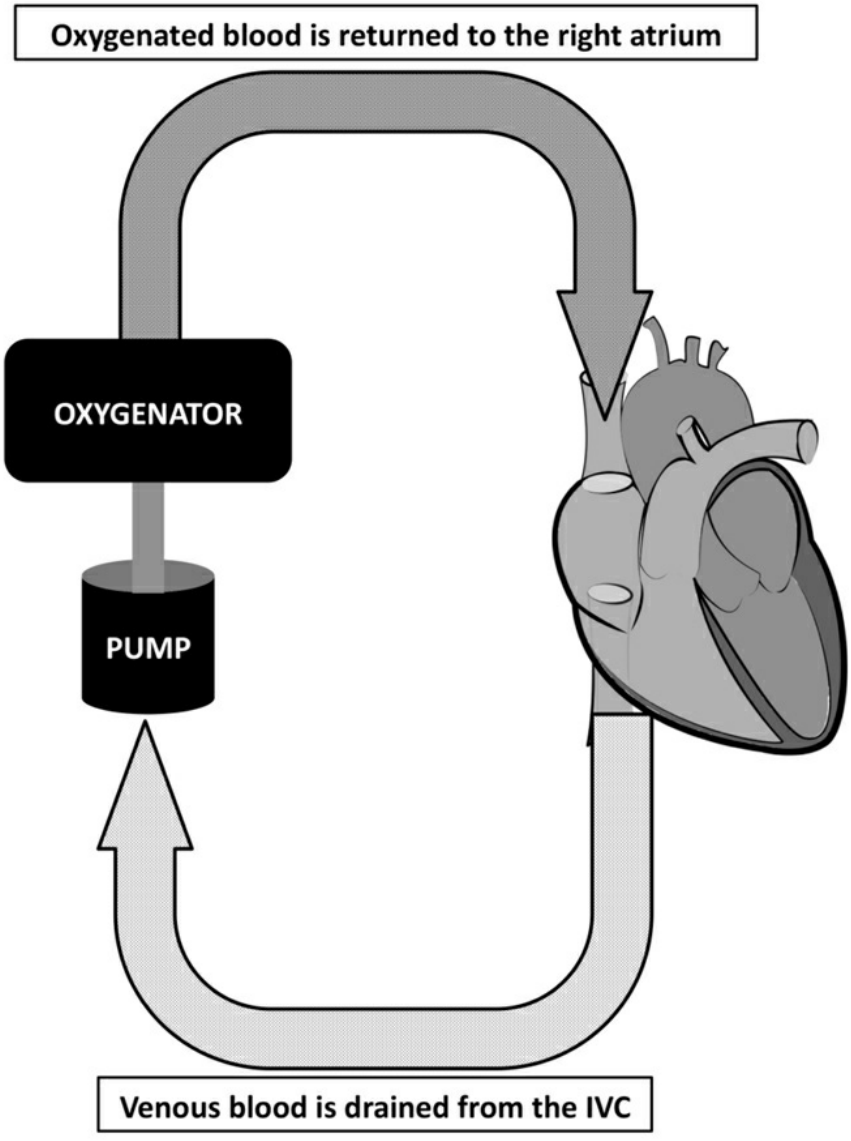
Veno-venous ECMO is considerably different from veno-arterial ECMO (VA ECMO). VA ECMO is similar to heart-lung bypass. Blood is drained from the venous side using a cannula placed in the femoral vein. The blood is pumped through an oxygenator, and the fully oxygenated blood is returned to the patient via a cannula placed in the femoral or subclavian artery. In neonates, the carotid artery is often used; in adults, however, the carotid artery is avoided due to the risk of stroke. With VA ECMO, the extracorporeal circuit can support both the pulmonary and the cardiac systems. The flow through the pump can make up for even the most severe heart failure. In fact, the primary indication for VA ECMO in adults is refractory cardiogenic shock.



The VA ECMO circuit provides both respiratory and cardiac support by pumping oxygenated blood directly into the aorta. The pump flow is sufficient to replace the entire cardiac output, if necessary.

VV ECMO, on the other hand, provides no cardiac support. Blood is drained from the inferior vena cava through a cannula placed in the femoral vein. After being pumped through an oxygenator, the blood is returned to the

right atrium through a cannula placed in the internal jugular vein.



VV ECMO provides respiratory support by oxygenating venous blood and returning it to the right atrium. Pulmonary blood flow is still dependent on the patient's own cardiac output.

Dual-lumen cannulas are also available, and function similarly to dual-lumen hemodialysis catheters (albeit much larger, to accommodate a flow of 4-7 L/min). The dual-lumen cannula is placed via the right internal jugular vein. It passes through the superior vena cava and into the inferior vena cava. The siphon, or drainage, ports are at the tip of the cannula in the IVC. Using

transesophageal echocardiography, the cannula is manipulated so that the return port is directed over the tricuspid valve. This helps reduce the risk of recirculation.

How VV ECMO Provides Respiratory Support

The best way to visualize VV ECMO is to consider the entire circuit as an extension of the right atrium. Normally, venous blood returning to the right atrium has an SvO_2 of 70-80%. In a markedly hypoxemic patient, the SvO_2 is much lower—50-60% is the norm. The venous blood goes through the pulmonary vascular system, where oxygen is picked up and CO_2 is unloaded (and ventilated off). Obviously, if a patient has severe ARDS, then the degree to which this gas exchange can occur is quite limited. Blood with an SvO_2 of 50% may only rise to an SaO_2 of 80%, even while the patient is breathing 100% oxygen and receiving high levels of PEEP.

When VV ECMO is initiated, some (but not all) of the venous blood is siphoned into the circuit. A pump drives a blood flow of 47 L/min through a membrane oxygenator. As the blood passes through the oxygenator, the hemoglobin becomes fully saturated and the PaO_2 may rise as high as 400-500 mm Hg. When this blood, with an SaO_2 of 100%, is returned to the right atrium, it mixes with the remaining venous blood and then proceeds through the pulmonary circulation. If half of the venous blood has an SvO_2 of 60% and the other half has an SvO_2 of 100% (thanks to the ECMO circuit), the total venous return going through the pulmonary circulation has an SvO_2 of roughly 80%. With higher pump flows, a greater percentage of the venous return is oxygenated using the ECMO circuit, leading to a higher overall SvO_2. In most patients, the ECMO flow can be increased to the point where the total SvO_2 is 8590%.

Here’s where VV ECMO becomes really cool. It’s also where you have to remember the principles of oxygen delivery [see the earlier chapter in this book]. With a high enough cardiac output and hemoglobin, oxygen delivery to the tissues can be maintained even with mild-to-moderate hypoxemia. In other words, an SaO_2 of 8085% is perfectly fine so long as cardiac output is sufficient and there is enough hemoglobin to carry the bound oxygen.

If an SaO_2 of 80-85% is enough to get the job done (with adequate

cardiac output and hemoglobin), and if the SvO_2 can be kept at 80-85% with VV ECMO, then **there is no need for pulmonary gas exchange whatsoever.** This is a very important point and is the cornerstone to understanding why VV ECMO can be an effective rescue therapy for severe ARDS. If the venous blood has an SvO_2 of 85% and it flows through lungs that contribute absolutely nothing, then the blood reaching the left atrium will have an SaO_2 of 85%. Since we've already established that an SaO_2 of 85% is sufficient if there's adequate cardiac output and hemoglobin, then there is no need to "beat up the lungs" with high PEEP, high ventilator rates, or any of the other usual things that are done for severe respiratory failure. Instead, the ventilator can be put on what are generally considered "rest settings."

Ventilator Rest Settings on VV ECMO[*]

- Pressure Control Ventilation
- Rate 10 breaths/minute
- I-time 1.0-2.0 seconds, adjusted for comfort
- P_{INSP} 25 cm H_2O
- PEEP 10 cm H_2O
- FiO_2 30%

Gas exchange in the ECMO circuit is a function of blood flow through the oxygenator and the gas flow of oxygen across the oxygenator's membrane. The oxygen that is flowing across the membrane is known as the sweep gas because it "sweeps off" CO_2 from the blood in the membrane. CO_2 has a much higher solubility than oxygen, and so it can be rapidly eliminated by increasing the sweep gas flow. Oxygenation can be increased by raising the rate of blood flow through the membrane oxygenator. Put simply, circuit flow controls oxygenation, while the flow of sweep gas controls ventilation. Sweep gas is usually 2-6 L/min. The FiO_2 of the sweep gas is initially set at 1.0 in order to attain the best oxygenation of the blood in the circuit.

Initial VV ECMO Settings

- Circuit blood flow of 50-60 mL/kg
- Adjust circuit flow to keep patient SaO_2 80-85%
- FiO_2 on sweep gas of 100%
- Set the sweep gas flow about the same as the circuit flow
- • Adjust sweep gas flow to keep $PaCO_2$ 35-45

Most of the time, some ventilator support is necessary. This isn't to provide additional gas exchange support, but instead to improve patient comfort and to prevent complications. If a patient is put on VV ECMO and then extubated, the lack of any positive pressure on the lungs will lead to near-complete alveolar collapse and consolidation. This can cause significant tachypnea and respiratory distress. Alveolar consolidation also prevents the normal clearance of secretions from the pulmonary tree, which can lead to pneumonia or lung abscess.

That said, recent experience with VV ECMO has shown that as patients recover, they can spend more and more time off the ventilator. This is important because it means that physical therapy and mobilization can begin early on, even while on VV ECMO. This is much easier with the dual-lumen cannula placed through the internal jugular vein. Early tracheostomy should be considered as soon as it's feasible in order to lessen sedation and begin mobilization. There is nothing like seeing a patient with severe ARDS walk down the hallway, with the ECMO circuit being pushed behind him.

Weaning VV ECMO

As the patient begins to recover, the FiO_2 of the sweep gas can be lowered. Circuit flow, once established, should not be lowered—lower blood flow increases the risk of thrombosis in the circuit. Keep in mind that VV ECMO is just like a really big right atrium. As the FiO_2 on the sweep gas is reduced, the blood flowing through the oxygenator will pick up less oxygen. That means that the proportion of gas exchange that has to occur through the

patient's lungs is increasing. Once the FiO_2 on the sweep gas is 0.21, the ECMO circuit is contributing nothing at all to the patient's oxygenation—it's all being done with low-level ventilator support. Blood is simply flowing through the big right atrium but there's no assistance with oxygenation. If the patient's condition is acceptable, it's time to come off ECMO.

Patient Selection

This is often the most difficult part of using VV ECMO for severe acute respiratory failure. For many years, ECMO was used predominantly for neonates with infant respiratory distress syndrome, meconium aspiration, and congenital diaphragmatic hernia. In recent years, however, ECMO has become more popular for older children and adults. The H1N1 influenza pandemic of 2009 accelerated the interest in ECMO, particularly VV ECMO, as a rescue therapy. The CESAR trial, published in *The Lancet* in 2009, demonstrated a survival benefit for patients with severe influenza-related ARDS transferred to ECMO centers.[69] Only 75% of those randomized to the ECMO arm actually received ECMO, which is an interesting finding. It may be that the true benefit was treating patients in high-volume centers with the appropriate expertise and ability to provide rescue therapies, including ECMO, rather than the provision of ECMO itself.

Indications for VV-ECMO

- Hypoxic respiratory failure with a predicted mortality risk ≥ 50%
  a. PaO_2/FiO_2 < 150 on FiO_2 > 90% despite optimal care for 6 hours or more
  b. Murray Score[*] ≥ 3 despite optimal care for 6 hours or more
- Hypercapnic respiratory failure refractory to treatment with pH < 7.15
- Acute onset of a potentially reversible cause of respiratory failure
- Age ≤ 65
- Immediate respiratory collapse that is unresponsive to optimal care (obstructed airway, etc.)

Contraindications to VV-ECMO[†]

- Mechanical ventilation at high settings (e.g. $FiO_2 \geq 90\%$, $P_{PLAT} > 30$, $PEEP \geq 15$) for 7 days or longer
- Contraindication to anticoagulation
- Absolute neutrophil count < $500/mm_3$
- Major CNS damage or other nonreversible comorbidity
- Age > 65
- Progression of chronic respiratory disease to the point of respiratory failure

Prior to initiation of VV-ECMO, the following steps should be taken to improve the patient's condition. These are listed in order of preference, although not all are required prior to cannulation for ECMO.

1. Lung protective ventilation using a tidal volume of 4-6 mL/kg predicted body weight, with PEEP according to the ARDSNet study protocol
2. Airway pressure release ventilation, with a P_{HIGH} up to 35 cm H_2O
3. Prone positioning for 16 hours, followed by supine positioning for 8 hours
4. Diuresis or CRRT to within 105% of dry weight, if hemodynamics permit
5. Bronchoscopy with therapeutic aspiration of the tracheobronchial tree

If the patient has not improved with the aforementioned therapy, VV ECMO team should be considered. Additional rescue maneuvers that can be tried include:

6. Inhaled nitric oxide
7. High frequency oscillatory ventilation

The Extracorporeal Life Support Organization (ELSO) provides extensive expert guidelines for patient selection and referral at its website: www.elso.org.

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* Always remember that the whole point of VV ECMO for respiratory failure is to let the lungs rest and recover. If they look whited-out on the CXR and the tidal volume on these settings is < 100 mL, so be it! Resist the temptation to use the vent for gas exchange. Let the ECMO circuit do the work.

* http://cesar.lshtm.ac.uk/murrayscorecalculator.htm

† Contraindications are relative, not absolute; however, the presence of these conditions is associated with a higher risk of treatment failure.

Chapter 21
Veno-Arterial ECMO

ECMO Management of Gas Exchange

The gas exchange function of VA ECMO is identical to VV ECMO. The function of the pump and the membrane oxygenator is the same in both modes. Therefore, the maneuvers used to address inadequate oxygen delivery with VV ECMO can also be used with VA ECMO. Increasing the FiO_2 on the circuit and increasing the flow through the circuit will both increase systemic oxygenation.

The primary difference relates to the location of the return cannula. With VV ECMO, the oxygenated blood is returned to the venous circulation, where it mixes with deoxygenated blood before entering the pulmonary arteries. If there is minimal gas exchange by the diseased or injured lungs, then the blood flowing into the left atrium and subsequently into the systemic arterial circulation will also be relatively deoxygenated. A typical SaO_2 for a VV ECMO patient is 80-85%. This is acceptable, so long as cardiac output and the hemoglobin level are sufficient to maintain oxygen delivery, but it requires ICU staff to recalibrate their expectations and not be alarmed by an SaO_2 below 90%.

With VA ECMO, on the other hand, the oxygenated blood is pumped into the arterial circulation. Most VA ECMO patients will have a normal SaO_2 of 95-100%, which makes the ICU staff very happy. Despite the normal SaO_2, however, systemic oxygen delivery may not be sufficient if cardiac function is poor, ECMO flow is insufficient, or if the oxygen consumption is increased. It is essential that the clinicians caring for patients on ECMO realize that there is much more to oxygen delivery than the SaO_2.

Ventilator Management on VA ECMO

The ventilator management in VV ECMO is quite easy—let the circuit do the heavy work, and use the ventilator to simply keep the lungs open without injuring them. It is quite common for the tidal volume to be less than 100 mL while on the rest settings, and that's fine—after all, the whole point of VV ECMO is to let the patient's lungs rest and recover. As long as the heart can maintain adequate cardiac output, VV ECMO can be used to support the respiratory demands.

Veno-arterial (VA) ECMO, on the other hand, is used for both cardiac and respiratory support. The ventilator management is different and it's essential to understand the mechanism of the extracorporeal circuit and the underlying physiology of cardiac failure.

Ventilator Settings and Goals on ECMO

VV ECMO

- **FiO_2 0.3-0.5**
- **PEEP 10**
- **P_{INSP} 10-15**
- **Accept dramatically low tidal volumes**
- **Priority is lung rest and recovery**

VA ECMO

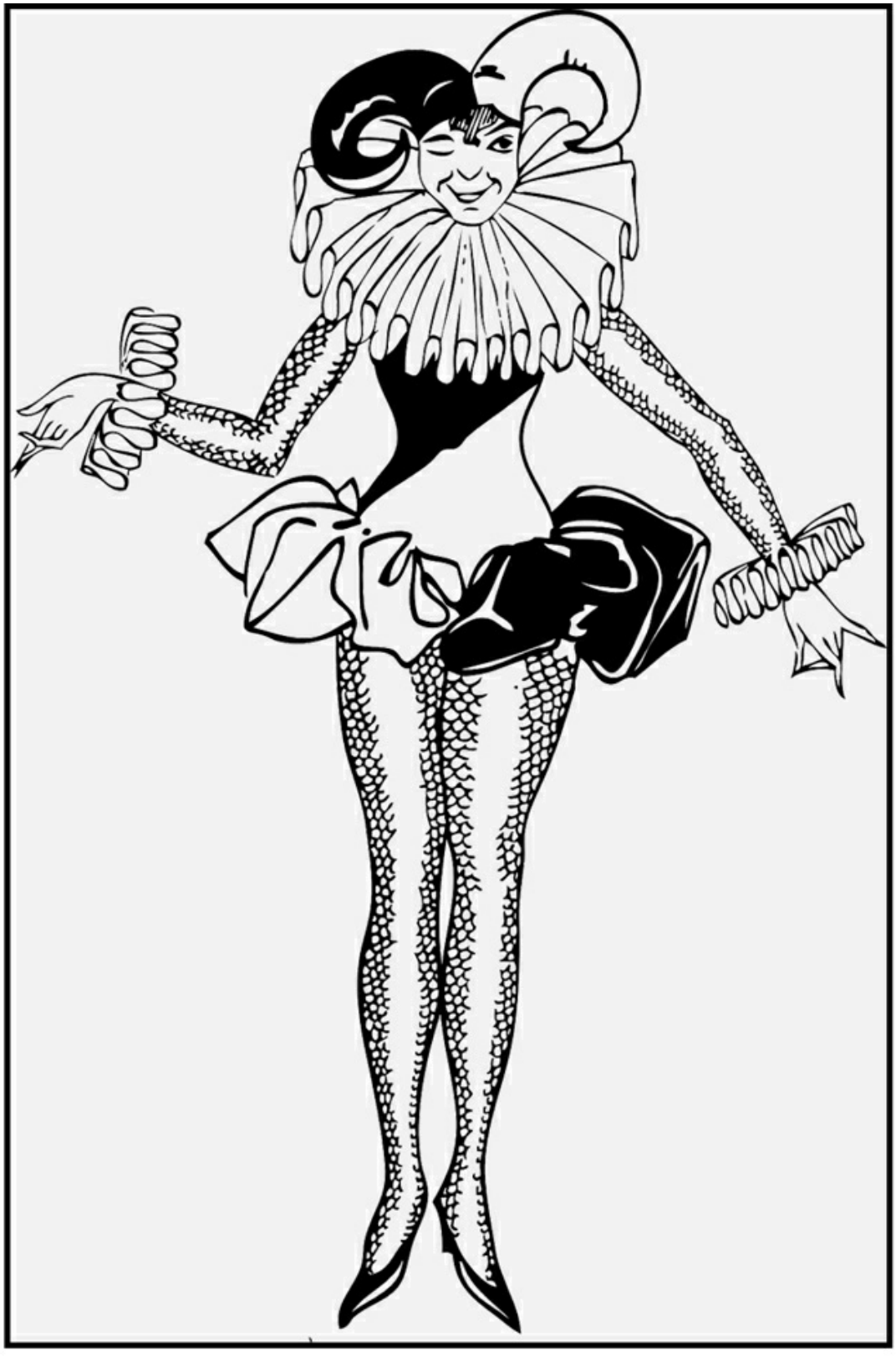
- **Tidal volume of 6-8 mL/kg**
- **PEEP and FiO_2 based on the ABG from the right radial artery and the chest X-ray**
- **Priority is to maintain adequate oxygenation of the coronary arteries and cerebral circulation**

With VA ECMO, it's important to keep in mind that while the ECMO

circuit provides oxygenated blood into the aorta, the blood in the aortic root is more dependent on the patient's native cardiopulmonary function. That means that the blood flowing from the pulmonary circulation into the left atrium and left ventricle is delivered preferentially into the coronary ostia and the aortic arch. In other words, *oxygen delivery to the coronary arteries, cerebral circulation, and the upper extremities, still depends on the gas exchange occurring in the patient's lungs*. The rest of the body, particularly the lower thorax and abdomen, gets its oxygen delivery primarily from the ECMO circuit.

The exact degree to which different areas of the body are perfused depends on how strong the heart is. Consider a patient with zero native cardiac function. All of his arterial flow, including the coronary ostia, depends on the ECMO circuit flow. The oxygenated blood coming out of the ECMO circuit is fully saturated, and the blood is distributed throughout the arterial circulation at the output generated by the circuit. A pulse oximeter placed anywhere on the patient's body should read 100%. This may seem ideal—who doesn't want an SpO_2 of 100%? However, the heart is designed to contract, and periods of full cardiac standstill aren't good. Without at least some cardiac contraction, the blood in the pulmonary circulation and the heart itself is prone to clot despite the most aggressive anticoagulation.

As cardiac contractility increases, the native heart will begin pumping blood into the aortic arch. As the heart grows stronger, it will perfuse more and more blood to the coronary arteries and the vessels coming off the aortic arch. The "mixing cloud" where ECMO flow meets cardiac flow moves progressively more distal, especially if the arterial return cannula is in the femoral artery with its tip in the distal aorta*. This can lead to a situation where the lower half of the body is well-oxygenated by the ECMO circuit, while the upper body (including the brain) is relatively hypoxic. There may be significant discrepancy between a pulse oximeter on the patient's forehead and one on his great toe, and in extreme cases there may even be apparent upper body cyanosis. This is known as the "Harlequin Syndrome."



A Harlequin clown, with contrasting colors on her costume

There are a few ways to treat the Harlequin Syndrome. The first, and most important, is to make sure that the patient is receiving adequate mechanical ventilator support. Making sure that a sufficient amount of PEEP and FiO_2 is provided will ensure that the deoxygenated blood flowing from the right ventricle to the lungs is adequately oxygenated by the time it returns to the left atrium. With VA ECMO, "usual" ventilator management (and not the "rest settings" used with VV ECMO) is most appropriate. Set the ventilator as if you were treating a patient with congestive heart failure. That means using a higher amount of PEEP if there is pulmonary vascular congestion. Since you cannot measure the PaO_2 directly from the coronary ostia, you'll need to measure it at the closest convenient site. After the coronary ostia, the next branch off the aortic arch is the right brachiocephalic artery. A blood gas specimen from the right radial artery will give an accurate measure of the native heart's oxygen delivery. If at all possible, VA ECMO patients should have a right radial arterial line. The exception would be with central cannulation via the right axillary or subclavian artery—then, a left radial arterial line should be placed. Of course, with central cannulation, Harlequin Syndrome is not an issue.

In order to ensure that the blood being pumped by the left ventricle (and received by the coronary arteries) is adequately oxygenated, target a PaO_2 of 80-100 mm Hg on the arterial blood gas specimen obtained from the right radial artery. Even if this sample reflects some mixture with the blood from the ECMO circuit, the oxygen delivery at the coronary ostia should be sufficient.

If the Harlequin Syndrome persists despite mechanical ventilator support, look at the chest X-ray. Any process causing hypoxemic respiratory failure can cause the Harlequin Syndrome, so it's important to find and correct anything reversible. This can include diuresis for volume overload, antibiotics for pneumonia, and bronchoscopy for lobar atelectasis. If the problem is poor cardiac function leading to pulmonary edema, then venting of the left ventricle may be necessary.

If the hypoxemia cannot be corrected with ventilator maneuvers or other measures, then it's time to take a page from the VV ECMO playbook and to dump oxygenated blood directly into the right atrium. This will increase the oxygen saturation of the blood going through the pulmonary circulation and into the left atrium. This hybrid mode of ECMO is known as VA-V (veno-arterial-venous) and requires a smaller cannula to be inserted into the internal

jugular vein. Once inserted, this cannula is connected with a T-adapter to the arterial return limb of the ECMO circuit. Fully oxygenated blood will be pumped from the membrane oxygenator into both the distal aorta (for systemic oxygenation) and the right atrium (for pulmonary oxygenation).

Left ventricular overdistension, with resulting pulmonary edema, is a common cause of hypoxemia during VA ECMO. Before jumping to VA-V ECMO as a solution, make sure that the left ventricle doesn't need to be vented. Clinically, left ventricular overdistension features pulmonary edema, high pulmonary artery occlusion pressure, and poor pulsatility on the arterial waveform. Harlequin Syndrome, on the other hand, is characterized by good pulsatility and improving cardiac function. The mixing cloud is moving distally as the heart gets stronger.

Hemodynamic Management of VA ECMO

The primary goal of VA ECMO is to provide adequate perfusion and oxygenation of organ systems while allowing the diseased or damaged myocardium time to recover. If recovery does not occur, then VA ECMO can be used as a bridge to a durable left ventricular assist device or heart transplant.

Typically, the circuit flow is adjusted to maintain a pulse pressure of at least 10-15 mm Hg, with inotropic support as needed, but there is little evidence to support this practice. Additionally, a recent trial showed an increased mortality in patients receiving epinephrine while on VA ECMO.[70] This was likely due to the increased myocardial oxygen consumption induced by an epinephrine infusion, which offset any benefit the ECMO circuit provided.

If the left ventricle gets overdistended, which is common with decompensated cardiac failure, then it can lead to poor contractility and hemorrhagic pulmonary edema. The increase in left ventricular end-diastolic pressure can also reduce the coronary perfusion pressure, leading to myocardial ischemia. Preload and afterload reduction are necessary to offload the left ventricle. Preload reduction can be achieved by increasing the ECMO circuit flow, diuresis, or ultrafiltration. Afterload reduction can be achieved pharmacologically, with nicardipine or nitroprusside; it can also be achieved mechanically with an Impella device or percutaneous septostomy. Inotropes are used to augment left ventricular output, with dobutamine and

levosimendan (not available in the United States) being the most commonly used agents. Reducing the ECMO circuit flow can also lower afterload, but this has to be balanced with the need to provide systemic perfusion of oxygenated blood. Allowing the mean arterial pressure to stay on the low side (50-60 mm Hg, so long as systemic perfusion seems adequate) will help with left ventricular emptying.[71]

The pulmonary artery catheter has gotten a bad rap in recent years, and it is not necessary to care for the majority of ICU patients. In the case of decompensated cardiac failure, however, the PA catheter can provide essential information for the treating clinician. This is especially true with VA ECMO. Knowing the SvO2, the pulmonary artery pressure, and the pulmonary artery occlusion pressure (as a surrogate for left atrial pressure) will help you find the right balance between volume status, left ventricular function, and circuit flow.

Hemodynamic, Respiratory, and Metabolic Goals for VA ECMO

- Mean arterial pressure 50-90—lower is better, as long as perfusion is acceptable
- Pulse pressure > 10
- SvO_2 > 65%
- DO_2:VO_2 > 3
- Lactate in the normal range
- PaO_2 80-100 (SaO_2 95-100%) from the right radial arterial line

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* With central cannulation via the axillary or subclavian artery, the regional oxygenation discrepancy is greatly reduced. This is because the cannula is returning oxygenated blood directly into the aortic arch or proximal aorta.

Chapter 22

Liberation from Mechanical Ventilation

Liberation has replaced weaning as the preferred term for getting patients off the ventilator. This is because, for the most part, prolonged weaning is unnecessary. Weaning refers to a gradual reduction in ventilator support, either by reducing the rate in SIMV or by reducing the pressure support in PSV. Liberation, on the other hand, implies that the patient is assessed daily for his readiness for extubation and then extubated when he meets the proper criteria.

In order to extubate a patient safely, there are a few conditions that have to be satisfied. First, the reason for extubation needs to have resolved or been corrected. If a patient is intubated for altered mental status, he should be awake and able to follow directions. If he was intubated for pulmonary edema or shock, he should have clear lungs and be off vasopressors. And so forth.

Second, the patient should be able to maintain adequate gas exchange without positive pressure ventilation. The criteria most commonly used are an $FiO_2 \leq 50\%$ and a PEEP ≤ 8 cm H_2O. Dynamic hyperinflation should not be present, and he should be able to maintain normocapnia without a very high minute ventilation (e.g., less than 10 liters per minute).

Third, he should have adequate cardiovascular reserve to tolerate unassisted breathing. Myocardial ischemia and reduced left ventricular function impair a patient's ability to breathe without assistance. Cardiogenic pulmonary edema benefits from the reduction in preload and afterload brought on by positive pressure breathing, and extubation can aggravate this.[72] A spontaneous breathing trial using a T-piece instead of CPAP or PSV may be helpful to determine if a patient with left ventricular dysfunction is ready for extubation.

Mental status is often a consideration when considering readiness for extubation. Patients who are stuporous or comatose have difficulty maintaining adequate airway tone and may have diminished protective reflexes, so aspiration and pneumonia are potential risks. In addition, patients with brain illness or injury can have disorders of central respiratory drive. Nevertheless, one study demonstrated that brain-injured patients who had no other reason to stay intubated other than mental status—that is, they didn't have high oxygen requirements, weren't being suctioned frequently, and didn't have periods of apnea—actually did better with early extubation.[73]

Weaning Parameters

Several clinical indices are commonly used to assess readiness for extubation. These can be obtained at the bedside, without much need for specialized equipment.

MIP: maximal inspiratory pressure; also known as the negative inspiratory force (NIF). Healthy young men can generate a MIP of -120 cm H_2O; women can generate a MIP of -90. For intubated patients, a MIP of less than -30 is usually considered adequate.

FVC: forced vital capacity. Normal subjects have an FVC of 70-80 mL/kg. In intubated patients, an FVC of 10-15 mL/kg is considered sufficient for unassisted breathing.

Minute Ventilation: a minute ventilation of more than 10 liters per minute to keep a normal $PaCO_2$ is generally too much work for a patient to perform without assistance from the ventilator.

Weaning parameters have several drawbacks, however. The MIP and FVC depend on adequate patient cooperation and effort, and they are static measurements at one point in time. The minute ventilation is a dynamic

measurement over a period of time, but it may be affected by patient discomfort or agitation. None of these parameters have sufficient positive- or negative-predictive value by themselves, although they can be useful adjuncts to clinical decision-making. For the most part, weaning parameters have been replaced by the concept of the *spontaneous breathing trial*.

Spontaneous Breathing Trial

A spontaneous breathing trial (SBT) is performed by observing a patient's respiratory efforts over a period of time, usually 30-120 minutes, with low or no ventilator support. One of the first major trials to show the utility of the SBT required putting the patient on a T-piece—oxygen tubing attached to the end of the endotracheal tube, which looks like the letter T.[31] The T-piece trial has the advantage of testing the patient's breathing without any ventilator support. It can be labor-intensive, though, and it's difficult to measure the tidal volume without a special device attached to the tube.

Other trials have shown that either CPAP alone,[74] or CPAP with the addition of low-level pressure support (5-8 cm H_2O)[75,76] are as effective as a T-piece SBT. Using CPAP or PSV has the advantage of letting you see the rate and tidal volume and not requiring disconnection from the ventilator.

At the conclusion of the SBT, assess the patient's readiness for extubation. Much of this is by a simple clinical examination—the person who is tachypneic, tachycardic, and diaphoretic is not ready; the person who is breathing slowly and deeply and seems comfortable probably is. In order to assist you, there's an index called the *Rapid Shallow Breathing Index*, or RSBI. This is the ratio between the patient's respiratory rate and the tidal volume (in liters). It's easier to breathe fast than deep, so a patient without a lot of respiratory muscle strength will take fast, shallow breaths. Slow, deep breaths are better. As an example, a patient with a respiratory rate of 10 and a tidal volume of 500 mL has an RSBI of 20 (10/0.5). Another patient with a respiratory rate of 50 and a tidal volume of 100 mL has an RSBI of 500 (50/0.1). Both have the same minute ventilation (10 L/min), but the latter patient is clearly not ready for extubation.

An RSBI of < 105 is predictive of successful extubation.[77] Since I do SBTs on the vent with PSV, I use a slightly stricter threshold of 80 to account for the assistance provided. You have to use some common sense and clinical

judgment as well—someone with an RSBI of 75 who has a paradoxical breathing pattern and is gasping will probably not do too well off the vent. Another person with an RSBI of 110 who otherwise looks calm and seems comfortable may in fact do well, and it could be worth giving her a chance.

An SBT should be done on every patient who meets the criteria. In order to be effective, the SBT assessment should be an automatic thing for all ventilated patients unless there's a specific reason not to (like an open chest, or high intracranial pressure, or a difficult airway). Ideally, the respiratory therapist will conduct the SBT at the same time that the nurse does the daily sedation vacation—this will improve your odds at getting patients extubated quickly. Remember that the ventilator is not therapeutic, and that the patient will come off the vent when he's ready. The purpose of the SBT is to recognize when he's ready and to not make him spend any more time on the vent than is necessary.

Daily SBTs have two advantages—first, they are simple to do. A daily assessment and spontaneous breathing trial take up a short amount of time and gives you a reliable way to know who can be extubated and who cannot. Second, they are the most effective way of liberating patients from mechanical ventilation. Daily SBTs have proven superior to SIMV and PSV "weaning" in terms of time on the ventilator and length of stay in the ICU.[72]

There are two types of days for patients with respiratory failure—vent days and get-off-the-vent days. A daily spontaneous breathing trial lets you know which kind of a day it is. If the patient passes, extubate! If not, put him back on assist-control ventilation. There's no benefit from "working him out" or by finding the level of support just above that where he fatigues. Let him rest and try again tomorrow. This method is simple. It's easy to make a part of your daily practice in the ICU. And it works.

Daily SBT Protocol

Assessment Criteria

$FiO_2 \leq 50\%$
PEEP ≤ 8
Able to follow directions

Not requiring frequent suctioning Hemodynamically stable
Not a known difficult airway
Not on unconventional ventilation (APRV, HFOV)
No physician order for "No Daily SBT"

If all of the assessment criteria are met, begin the Spontaneous Breathing Trial

1. CPAP 5 cm, PS 7 cm for 30-60 minutes
2. At the end of the SBT, calculate the RSBI
3. If the RSBI is < 80, extubate the patient
4. If the RSBI is > 80, back to assist-control
5. If there is concern over the patient's readiness for extubation, call the physician

Abort the SBT for any of the following

Desaturation below 88%
Increase in heart rate by 20 beats/min
Significant change in blood pressure
Diaphoresis
Accessory muscle use or paradoxical breathing pattern

Chapter 23

Prolonged Respiratory Failure

About 20% of ventilated patients will not be able to liberate quickly once their illness or injury resolves. This may be due to preexisting illnesses, poor cardiac function, chronic lung disease, malnutrition, deconditioning, or critical illness polyneuromyopathy. A good definition of prolonged respiratory failure, or difficult weaning, is when the patient is still intubated after at least three spontaneous breathing trials and more than seven days after resolution of the acute illness or injury.[72]

Timing of tracheostomy

Timing of tracheostomy placement is controversial and varies widely between institutions and practitioners. While many critical care physicians would agree a tracheostomy should be performed after two weeks of respiratory failure, there are a substantial number who believe that this is too long to wait. The literature is divided on the topic—some studies have shown a benefit,[78] while a recent multicenter randomized trial showed no advantage to early tracheostomy.[79] In this trial, a significant number of patients randomized to tracheostomy at 14 days were extubated prior to the operation, suggesting that waiting is not necessarily a bad thing.

Benefits of earlier tracheostomy include patient comfort, increased mobility, less need for sedation, and a shorter time in the ICU. Drawbacks of tracheostomy include the need for an invasive procedure, the risk of tracheal stenosis, and the psychological burden it places on the patient (since many people associate a tracheostomy with chronic illnesses like cancer). There is a psychological shift among caregivers as well, in my experience—for some patients, once a tracheostomy is placed that person becomes a “trach patient.” Physicians and nurses seem to be more likely to send a “trach patient” to a

nursing home, and there can be a reluctance to decannulate (i.e., remove) the tracheostomy tube, even after the patient is liberated from the ventilator.

Like everything else, this decision needs to be individualized for the patient. If prolonged ventilation is anticipated due to neurologic illness or injury or because of airway obstruction, then tracheostomy should occur rather quickly. On the other hand, if the disease process is one where you expect recovery within one to two weeks (chest or abdominal trauma, pneumonia, status asthmaticus, CHF exacerbation), then I would wait.

Removing the Tracheostomy

Once the patient is free of the vent, it's time to begin thinking about decannulation. This, obviously, depends on many factors and there is no specific rule regarding when a tracheostomy tube can be removed. Some general requirements for decannulation are:

1. The patient should be able to get out of bed and get around (even with a wheelchair).
2. He should be able to speak and breathe comfortably with the tracheostomy tube occluded (e.g., with a Passy-Muir® Speaking Valve).
3. There should be no need for frequent suctioning or other pulmonary toilet measures.
4. There should be no anticipated need for positive pressure ventilation.

Contributors to Prolonged Respiratory Failure

Many of the reasons why patients are ventilated are self-evident and should be treated. The following list mentions some that may not be as obvious. Dynamic hyperinflation, delirium, diaphragmatic paralysis, hypothyroidism and neuromuscular disease are all good examples of relatively common occult conditions leading to prolonged respiratory failure.

Pulmonary: dynamic hyperinflation, diaphragmatic paralysis, pulmonary fibrosis

Cardiac: impaired left ventricular systolic function, pulmonary hypertension, pericardial effusion, constrictive pericarditis

Neurologic: brainstem lesions, cervical spine injury or disease, neuromuscular disease

Endocrine: hypothyroidism, hypoadrenalism, low testosterone (in men)

Malnutrition

Critical Illness Neuromyopathy

Deconditioning

Delirium

Nutritional Support

Adequate caloric and protein intake via the enteral route is a tenet of critical care medicine. For most patients in the ICU, nutritional needs can be estimated—25-30 kcal/kg from carbohydrates and fat, with 1-1.5 g/kg protein. For people with prolonged respiratory failure, I do a more detailed evaluation of their nutritional regimen every one to two weeks.

A balanced diet yields a respiratory quotient (RQ) of 0.8. The RQ represents the body's CO_2 production divided by its O_2 consumption. Different food sources have a different RQ—a diet consisting solely of fat would have an RQ of 0.7, while a carbohydrate-only diet has an RQ of 1.0. If the RQ is too high (0.85 or higher), it can lead to excessive work of breathing; after all, the lungs are the organs that have to clear all of the CO_2 produced by metabolism. A metabolic cart study can be used to determine the RQ. If it exceeds 0.9, I switch to a lower-carbohydrate tube feeding formula.

The metabolic cart study can also calculate the resting energy expenditure (REE) in kcal/day. There are many formulas for predicting how many calories over the REE a patient needs. I try to keep it simple and provide about 500 kcal above the REE, and I try to provide all of the patient's caloric

needs with carbohydrates and fat (in a 60/40 ratio, to keep the RQ down). That way protein can be used to build muscle instead of being burned for energy.

Most of the nitrogen byproducts of protein metabolism are excreted in the urine. About 2g N are lost in the stool, and another 2g are lost through the skin. A 24-hour urine urea nitrogen (UUN) collection tells you how much is lost in the urine. Adding these up, we know the patient's daily nitrogen excretion. Since protein is 16% elemental nitrogen, multiplying the total daily nitrogen excretion by 6.25 gives the amount of protein, in grams, necessary to break even. In order to provide enough protein for skeletal muscle anabolism, I try to give about 10-20 grams of protein above this. For example, if a patient has a 24-hour UUN of 10g N, his daily excretion is 14g (10 from the urine, 2 from the stool, 2 from the skin). Multiplying 14 by 6.25 gives us 87.5g protein needed to break even. Therefore, I would make sure he's taking in about 100 grams of protein a day.

Critical Illness Neuromyopathy

This condition is fairly common in the ICU. Drugs associated with critical illness neuromyopathy include aminoglycoside antibiotics, corticosteroids, and neuromuscular blocking agents. Prolonged neuromuscular blockade with concurrent high-dose steroid therapy is one of the leading causes of this condition. Clinically, it's manifested by weakness and diminished reflexes. Physical exam findings can range from mild weakness to tetraparesis. Facial innervation is usually spared. Electromyography is confirmatory, but the appropriate clinical history is usually sufficient to make the diagnosis. Critical illness neuromyopathy can hamper efforts to get the patient off the vent. Unfortunately, there is no treatment for this other than good physical therapy and time.

Delirium

Delirium can fall into two types—hyperactive and hypoactive. Hyperactive delirium is the kind that gets the most attention and the most late-night phone calls. Hypoactive delirium is less obvious but is still a problem. Both types can lead to prolonged respiratory failure, usually because of concerns for the patient's ability to protect his airway.

Delirium can be due to the patient's primary illness, medications, or environmental factors in the ICU. Important reversible causes of delirium include sepsis, alcohol withdrawal, stroke, myocardial ischemia, pulmonary embolism, and pain. All of these should be sought out if indicated and treated. Some patients are very difficult, if not impossible, to ventilate without heavy sedation. Tracheostomy can be beneficial, since the tracheostomy tube is much more tolerable than the endotracheal tube and the amount of sedation can be reduced.

Medications are another important cause of delirium. Prolonged benzodiazepine use, either by continuous infusion or intermittent dosing, can cause paradoxical agitation and confusion. Benzodiazepine infusions may make a patient look asleep, but there's very little REM sleep actually occurring. H2-receptor blockers and fluoroquinolones have also been implicated, especially in the elderly. Dexmedetomidine has been studied as a sedative for mechanically ventilated patients and seems to be associated with less delirium when compared with benzodiazepines.

Environmental factors can lead to the so-called "ICU psychosis," which I believe is a fancy term for sleep deprivation. It's very difficult to get a good night's sleep in the intensive care unit, and this is made worse by blood draws, fluorescent lights, alarms, and all of the other sights and sounds of a modern ICU. Every attempt should be made to permit patients to sleep at night. Minimizing nocturnal blood draws, unless they are truly necessary, is a good start. Turning out the lights and reducing ambient noise can also help.

Mobility

It seems like common sense that ICU patients who are comatose, are in shock, or who have severe respiratory failure should remain on bedrest. What's not acceptable, however, is for a person to spend day after day flat on his back even after he's started to recover from his illness. Lying in bed all day is not healthy. Moreover, prolonged bedrest is associated with decubiti, deep venous thrombosis, atelectasis, pneumonia, muscle wasting, and other bad things.

There are no reasons why the majority of intubated patients should not get out of bed. It will take some assistance from the ICU staff, but it is definitely possible. The benefits are both physical and psychological. Sitting upright, or standing with assistance at the bedside, strengthens core muscles

and helps prevent the muscle wasting often seen in critically ill patients. Atelectasis is reduced with positional changes and pulmonary gas exchange improves. Walking is also a possibility—you can either bag the patient through the endotracheal tube or push the ventilator behind him, since most vents have a battery and portable O_2 supply.

From a psychological standpoint, patients seem to need less sedation if they are able to move about and change position. Lying in bed all day may sound good to you, but that's if you can roll over, adjust your pillow, and sit up if you want to. When intubated patients try that, we tie them down with restraints and sedate them! It's also empowering—even a small amount of daily exercise can give people a sense of recovery.

I recommend that every patient in the ICU be evaluated by Physical Therapy. It's also important for the rest of the ICU staff to know that early mobility and walking are an important part of critical care and to make it part of the unit's daily routine. The only reasons why an intubated patient should not get out of bed are:

- $FiO_2 \geq 60\%$ or $PEEP \geq 10$
- Anatomic reason (fractured leg, open abdomen, open sternum, etc.)
- Coma
- Shock (on vasopressors)

That's it. Most ICU patients don't fall into these categories; therefore, most ICU patients should be moving!

Ventilator Weaning in Prolonged Respiratory Failure

Most patients who are intubated don't need weaning—they need a daily assessment and spontaneous breathing trial. For those who have failed this, however, some gradual reduction in ventilator support may be helpful. Unfortunately, there are no clinical trials showing benefit of one approach over another. Some centers use SIMV weaning, where the vent rate is reduced daily, and then the pressure support. Other centers use PSV during the day, adjusted to maintain comfortable breathing, with assist-control at night for respiratory muscle rest. Still others use periods of unassisted breathing (T-piece or trach mask) as tolerated, with assist-control ventilation in the event of fatigue.

Since the ventilator itself is not therapeutic, it really doesn't make sense that a particular mode of ventilation would prove to be superior. It does make sense that fatigue is harmful, so a protocolized approach with a gradual reduction in support should be better than going all-or-nothing. The most important factor is the standardization in a particular institution—the method of weaning is less important than having a method in the first place. If the vent weaning strategy varies wildly depending on which physician is rounding on a particular day, then it's going to be hard to have successful results.

In addition, attention to the non-respiratory things is important. Ensuring adequate nutrition, mobility, and preventing delirium is as fundamental as having a ventilator weaning strategy. Like everything else in critical care, the details matter.

Finally, be realistic. There will be good days, bad days, and setbacks. Don't get discouraged and don't let the patient get discouraged. It may be necessary to pause ventilator weaning for a few days, but it shouldn't lead to giving up in frustration. Stay positive!

SIMV with PS Ventilator Weaning Protocol*

- Assumes patient has a tracheostomy
- Tidal volume 8 mL/kg PBW when on SIMV
- FiO_2 30-50%, PEEP 5-8
- If the patient can't complete the step, return to the vent (if on trach collar) or go back 1-3 steps as needed (if on the vent) and try again the next day

Day	Trach Collar Time	Vent Settings
1	-	Rate 10, PS 20
2	-	Rate 8, PS 20
3	-	Rate 6, PS 20

4	-	Rate 4, PS 20
5	-	Rate 4, PS 18
6	-	Rate 4, PS 16
7	-	Rate 4, PS 14
8	-	Rate 4, PS 12
9	-	Rate 4, PS 10
10	1 hour	Rate 4, PS 10
11	2 hours	Rate 4, PS 10
12	4 hours	Rate 4, PS 10
13	6 hours	Rate 4, PS 10
14	8 hours	Rate 4, PS 10
15	10 hours	Rate 4, PS 10
16	12 hours	Rate 4, PS 10
17	16 hours	Rate 4, PS 10
18	20 hours	Rate 4, PS 10
19	24 hours	-
20	24 hours	-
21	24 hours	-

PRVC with Automode* Ventilator Weaning Protocol

- Assumes patient has a tracheostomy
- Tidal Volume 8 mL/kg PBW
- Rate 10
- FiO_2 30-50%, PEEP 5-8

Activate Automode (in PRVC on the Servo ventilator, this will be Volume Support)

In Volume Support, the ventilator will allow the patient to breathe spontaneously a la Pressure Support Ventilation but will adjust the inspiratory pressure as needed to reach the goal tidal volume. Think of it as an auto-adjusted pressure support.

As the patient's compliance and strength improve, it will take less pressure to get the goal tidal volume. The peak inspiratory pressure will drop accordingly.

If the patient's condition worsens, it will take more pressure to get to the goal tidal volume and the peak inspiratory pressure will increase accordingly.

Every day, put the patient on trach collar for as long as tolerated. Return to PRVC/Automode when he gets tired.

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* Modified from the TIPS Ventilator Weaning Protocol [*Chest* 2001 Jan; 119(1): 236-42.]

* For use with the Maquet Servo ventilator. This could be adapted easily to whichever ventilator you're using—for example, instead of Automode, you could use Proportional Assist. Read the instruction manual that came with the ventilator.

Chapter 24

Mechanical Ventilation during a Pandemic or Mass Casualty Event

This chapter was released to the public in 2020 during the height of the COVID-19 pandemic. It is a general outline of how healthcare workers can treat a large number of patients with respiratory failure, especially if expert consultation is limited. This chapter can be copied and distributed to whomever might use it to help critically ill patients. *Commercial use of this work is not permitted without the author's express written consent.*

At the time of this writing, the world has been afflicted with SARS-CoV-2, also known as COVID-19. The spread of this coronavirus has exposed the weaknesses of our healthcare system's ability to handle large numbers of critically ill patients. Many patients infected with COVID-19 will progress to ARDS and require mechanical ventilation. While VV ECMO is appealing, it is a very resource-intensive therapy that is not practical to implement on a wide scale. Therefore, it falls to intensivists and others to treat many patients at once with ventilators that may or may not be capable of advanced modalities.

During this kind of a pandemic, we need to remember the truism that *perfect is the enemy of good*. Our focus should be on saving as many lives as possible, and we won't have the luxury of being able to titrate every ventilator perfectly. As I write this chapter, patients with acute respiratory failure are being treated by healthcare practitioners with limited background in critical care medicine. They are doing the best they can with what they have. This chapter outlines my recommendation for how to best provide care to those infected with COVID-19, but it could easily apply to an outbreak of influenza or another infectious disease, or a mass casualty situation.

The first priority is to **protect the people providing care.** While it may

sound noble to rush to the aid of a patient, the most important resource in a pandemic is the supply of qualified healthcare workers. Personal protective equipment is mandatory for anyone caring for critically ill patients—mask, face shield, gown and gloves must be worn. Jeopardizing the health and safety of those committed to the task at hand cannot be permitted. Likewise, viral filters must be attached to all ventilators (both conventional and noninvasive), and rooms should be retrofitted to be negative pressure if at all possible. These measures will limit the transmission of the virus to healthcare workers and other patients.

The second priority in a situation where the number of patients needing critical care is stressing the capacity of the healthcare system is to follow the K.I.S.S. principle—**keep it simple, superstar.** Eliminate as many decision points as possible. Follow a plan that will work for 80% of the people, so you have the time and cognitive ability to deal with the 20% who don't respond or get worse. The concepts underlying this are discussed further, but if you want something that can be applied quickly to a lot of patients with acute respiratory failure, here it is:

GOALS
SpO_2 85-95%
P_{PLAT} 30 or lower

Assist-Control
Rate 16, Tidal Volume 6 mL/kg
FiO_2 0.5
PEEP 10

GETS WORSE?

Assist-Control
Rate 16, Tidal Volume 6 mL/kg
FiO_2 0.8
PEEP 15

GETS WORSE?

APRV
P_{HIGH} 30, P_{LOW} 0
T_{HIGH} 5.0 sec, T_{LOW} 0.8 sec
FiO_2 0.8

OR

PRONE POSITIONING

GETS WORSE?

EXPERT EVALUATION
CONSIDER VV ECMO
(if available)

If you follow this plan, the first two steps will work for most patients. The remainder will be supported with a switch to APRV or by utilizing prone positioning. Obviously, there will need to be some adjustments made to make sure the patients receive appropriate care, but I venture that this outline will serve as an acceptable "big picture" plan for providing mechanical ventilation in a crisis situation. This frees up the respiratory therapist to troubleshoot problems and frees up the critical care physician to devote his cognitive efforts to those who don't respond.

Basic Concepts

Instead of rehashing all of the concepts of lung protection and the pathogenesis of ventilator-associated lung injury, let's review just a few key concepts. This will guide treatment of patients and help streamline ventilator protocols.

- A tidal volume of 4-8 mL/kg of predicted body weight (PBW) is desirable in most patients. This is close to the normal resting tidal volume of 5-6 mL/kg PBW.
- Alveolar stretch (and potential for injury) is most closely reflected by the end-inspiratory pressure, held for 0.5-1.0 seconds. This is also known as the *plateau pressure* (P_{PLAT}). A P_{PLAT} higher than 30 cm H_2O is associated with an increased risk of lung injury, and some studies have suggested that the P_{PLAT} should be kept at 25 or lower.
- Oxygen is obviously necessary for life, and the FiO_2 often needs to be increased in the critically ill. That said, there is little if any benefit to "normalizing" the SaO_2 or PaO_2. A PaO_2 of 50-80 mm Hg, which corresponds with a SaO_2 of 85-95%, seems to be sufficient.
- On a related note, breathing 100% oxygen does cause absorption atelectasis, which could worsen shunting (areas of lung that are perfused but not ventilated). Maintaining some nitrogen in the alveoli will help stabilize them and prevent collapse. The FiN_2 should be at least 0.1, and ideally 0.4-0.5 if possible. That means the FiO_2 should ideally be no higher than 0.6.
- PEEP is used to recruit alveoli so they can participate in gas exchange, and to keep them open at end-expiration. This helps maintain the

functional residual capacity of the lung and improves oxygenation.

- Even though the term "stiff" is used to describe the lungs of a patient with ARDS, that isn't really the problem. The problem is that the lungs are small. The usable part, at least. Some areas of the lungs are normal, and some areas are damaged. The goal is to support the patient using the normal lung and to avoid causing further damage with excessive distending pressure or tidal volumes.
- If one breath with too high of a tidal volume can cause lung injury, then it follows that the more breaths, the more potential for lung injury. Keeping the respiratory rate lower may reduce the overall impact of mechanical ventilation on the patient's lungs. Respiratory acidosis is generally well-tolerated.

Initial Ventilator Settings

Having standardized initial ventilator settings during a pandemic or mass casualty situation is helpful because it provides what should be adequate support to a large number of patients without having to rely on a clinician coming up with an individualized plan for each person. The hidden truth is that this is what we already do, most of the time, anyway. This assumes that the primary problem is hypoxemia, and that the underlying lung pathology is one of acute alveolar damage (e.g., ARDS).

Mode: Volume Assist-Control, with decelerating flow if possible

Volume assist-control is the most commonly used mode and it's a good idea to stay with what people are comfortable with, at least to start. Decelerating flow is available on most ventilators, and the combination is known by different trade names—PRVC, VC+, CMV with Autoflow, APVcmv, etc.

Rate: 16 breaths/minute

This should provide a minute ventilation of about 100 mL/kg/minute, or 6-8 L/min, which is on the high end of the normal range. Remember that we're not that concerned about hypercapnia.

Tidal Volume: 6 mL/kg PBW

This is the commonly accepted starting point for lung-protective ventilation.

FiO_2: 50%, or 0.5

Why not 100%? First off, most patients don't need that much oxygen. This limits the number of adjustments that are needed. It also provides adequate alveolar nitrogen to keep alveoli open.

PEEP: 10 cm H_2O; 15 cm H_2O for BMI > 50

PEEP opens up alveoli and keeps them open, improving gas exchange and functional residual capacity. The more white stuff on the X-ray, the more PEEP you need. Heavier patients (BMI > 50) need more PEEP to counteract the increased restriction of their chest wall.

These settings should work for most patients, at least to start. Of course, some adjustments will be necessary. Follow these guidelines:

- Check the P_{PLAT} every 4 hours. Lower the tidal volume as needed to keep the P_{PLAT} at 30 or less. The purpose is to avoid overdistension and injury to the healthy alveoli.
- Check the end-expiratory pressure at the same time. If the measured PEEP exceeds the set PEEP by more than 2, then "autoPEEP" is present—the patient doesn't have enough time to exhale, and the alveoli are getting overdistended. Lower the rate to 10 or 12, giving more time for the air to get out.
- Keep the SpO_2 85-95%. This is more than enough to sustain life. There's no need to get frequent ABGs to measure the PaO_2 as long as you feel that the pulse oximeter is reliable, and the SpO_2 (surrogate for SaO_2) is much more important in terms of total oxygen delivery.[*]
- Keep the pH above 7.15, using sodium bicarbonate as needed. Otherwise, don't worry too much about hypercapnic respiratory acidosis unless the patient has issues with shock, intracranial hypertension, or severe pulmonary hypertension. Most patients tolerate a respiratory acidosis quite well. This keeps ventilator adjustments (and respiratory therapist exposures) to a minimum. It may also

prevent lung injury—every time the ventilator cycles, there's a possibility of injury, so keeping the rate lower should be helpful.

- Troubleshoot as needed, but keep in mind that **the ventilator is a means of support and will not do anything to make the patient get better any sooner.** Your goal is to keep the patient alive and to not make him worse with injurious ventilator settings until he recovers from the illness.

When the Patient Gets Worse

Many patients will remain hypoxemic despite using a PEEP of 10 and a FiO_2 of 0.4-0.6. If the SpO_2 remains < 85%, escalating ventilator support may be in order. The first, and easiest, thing is to increase the PEEP and FiO_2. Increasing the PEEP to 15 and the FiO_2 to 0.8 will help in many cases, especially if the ICU staff accepts the fact that a SpO_2 of 85-88% is OK. If needed, the PEEP can be increased to 20, but be careful—a PEEP at this level can compromise hemodynamics and adversely affect gas exchange if alveoli get overdistended.

APRV

If the patient is failing conventional ventilation, airway pressure release ventilation (APRV) is a reasonable next step. Most modern ventilators have an APRV mode (although they call it different things, like Bi-Vent or Bi-Level). APRV works by holding an inflation pressure for a prolonged time, usually 4-6 seconds, followed by a rapid depressurization of the circuit. The depressurization allows CO_2 to be eliminated from the alveoli, and the length of time of depressurization is short—0.5-1.0 seconds. The terminology for APRV can be confusing, but the concept is relatively simple.

- P_{HIGH}: The pressure that is maintained on the alveoli for the majority of the time. Think of this like you would CPAP. The pressure is usually 25-30 cm H_2O.
- T_{HIGH}: The time that the patient spends at P_{HIGH}.
- P_{LOW}: The pressure that the ventilator "decompresses" to. This is

usually zero, to permit maximal expiratory airflow, but it can be increased to 5-10 in cases of severe hypoxemia.

- T_{LOW}: The time that the circuit is depressurized, or released. This is short—0.5-1.0 seconds—so that the recruited alveoli don't collapse. It's short enough to get the CO_2 out, but not any longer than that. The T_{LOW} is usually adjusted to allow the peak expiratory flow to fall by about 50%. Any shorter, and CO_2 elimination will suffer. Longer than that (especially if flow falls to, or near, zero), and alveolar derecruitment will occur.

Ways to improve oxygenation in APRV:

- Increase the P_{HIGH}, up to 35
- Increase the FiO_2
- Increase the T_{HIGH}, which increases the mean airway pressure
- Increase the P_{LOW}, up to 10 (this will lead to a higher $PaCO_2$, but oxygenation is more important)

Ways to improve ventilation (CO_2 elimination) in APRV:

- Increase the P_{HIGH}—the higher the gradient between P_{HIGH} and P_{LOW}, the more gas is exhaled on the release
- Lower the T_{HIGH}—this increases the frequency of the releases
- Increase the T_{LOW}—this will allow more gas to be exhaled, but it risks alveolar derecruitment.

The primary advantage of APRV is that it increases the mean airway pressure, and oxygenation, without very high distending pressures. Holding the pressure for 4-6 seconds may recruit more alveoli without the strain of trying to inflate the lungs in a shorter time (like you do with conventional ventilation).

Prone Positioning

Prone positioning is a mainstay in the management of ARDS, and it has a

lot of advantages. Proning helps “homogenize” the lungs by preventing regional overdistension. It also helps with secretion clearance and it takes the weight of the abdominal organs off the thorax. Prone positioning also has no physiologic cost—it doesn’t increase work of breathing, energy expenditure, or cause additional stress or strain on the lungs (unlike APRV). So, why don’t we just prone everyone? The primary reason is related to potential healthcare worker exposure. It takes 4-6 people to safely prone a patient, twice a day. This requires available workers, and there is always the risk of pathogen transmission even with personal protective equipment. For this reason, proning should be considered only if APRV fails or cannot be used (hemodynamic instability with the higher pressure, bronchopleural fistula, etc.).

If prone positioning is done, the prone period should be 1618 hours, followed by a return to supine. Neuromuscular blockade and heavy sedation help keep the patient from dislodging tubes and lines but aren’t mandatory. Proning should continue until the PaO_2/FiO_2 ratio is greater than 150 when supine.

Therapies That Are Less Preferred

Inhaled nitric oxide should not be used simply for hypoxemia. There is no data supporting its use in ARDS. If there is significant right ventricular dysfunction and cardiogenic shock, then inhaled NO might be useful.

High frequency oscillatory ventilation can be used, but it is not preferred for several reasons:

- Availability of the HFOV units is limited.
- Monitoring the patient is difficult, particularly when respiratory isolation measures are in place—there are no alarms on the HFOV unit to let you know when the patient has a problem.
- APRV improves oxygenation by increasing the mean airway pressure, which is the same thing that HFOV does; APRV is easier to use and doesn’t require special equipment.
- Clinical trials have not shown a benefit from HFOV in ARDS, regardless of severity.

Other Things

Don’t forget about the other things that go into caring for the critically ill. While the focus right now is respiratory care, we need to make sure that we’re treating the patient as a whole.

- Nutrition should be provided early on, by the enteral route. Aim for about 25 kcal/kg/day of a commercially available formula, but don’t stress if the patient doesn’t tolerate full feeding. Just get something in the gut.
- Diuresis will help with oxygenation. Try to keep the patient within 5% of his normal body weight and avoid excessive fluid boluses. If hemodynamics are tenuous, the combination of albumin/furosemide can be helpful.*
- DVT prophylaxis—enoxaparin, or heparin if there’s renal dysfunction.
- Early mobilization once the respiratory and hemodynamic status of the patient has improved.
- Tracheostomy once the FiO_2 is down to 0.5 or less, the PEEP is down to 10 or less, and the patient is afebrile.

EPIDEMIC MECHANICAL VENTILATION PLAN

The purpose of this plan is to provide standardized ventilator settings for patients with presumed or confirmed infection with coronavirus, influenza, or another serious respiratory infection. It can also be used during a mass chemical or toxin exposure. Having a standardized plan should reduce the number of times that healthcare workers have to adjust ventilator settings and help prevent unnecessary exposure to respiratory secretions.

This plan is not intended to replace clinical judgment. Changing the ventilator mode or settings may be necessary for an individual patient, at the attending physician's discretion.

INITIAL VENTILATOR SETTINGS:

Mode: Volume Assist-Control, with Decelerating Flow

Rate: 16

VT: 6 mL/kg

FiO_2: 0.5

PEEP: 10

- Goal SpO_2 is 85-95%. There is no reason to increase the FiO_2 to get a SpO_2 higher than this range. Routine ABGs are not necessary and should only be ordered if it will lead to a significant change in strategy.
- Goal pH is > 7.15. Otherwise, hypercapnia is acceptable.
- Measure the end-inspiratory pressure q4h. If the P_{PLAT} is > 30, lower the VT until the P_{PLAT} is 25-30.
- Measure the end-expiratory pressure q4h. If the measured PEEP is > 2 over the set PEEP, lower the ventilator rate to 10-12 and increase the VT to 8 mL/kg.
- For moderate hypoxemia (SpO_2 < 85%) despite the above settings,

increase the PEEP to 15 and the FiO_2 up to 0.8.

For hypoxemia (SpO_2 < 85%) despite a PEEP of 15 and FiO_2 of 0.8, begin APRV:

- P_{HIGH} 30
- P_{LOW} 0-5, depending on degree of hypoxemia
- T_{HIGH} 5.0 sec
- T_{LOW} 0.8 sec—adjust for a drop in peak expiratory flow of 25-50%
- FiO_2 0.8

Prone positioning (16 hours prone, 8 hours supine) should be initiated if APRV cannot be used successfully. Inhaled nitric oxide should not be used for hypoxemia. It is reserved for the treatment of right ventricular failure in cardiogenic shock. Eye and mouth care is essential. Tube feeding in the prone position is permissible if the tube is post-pyloric; otherwise, hold tube feeding while prone and increase the rate of feeding while supine.

PRONE POSITIONING CHECKLIST

Indications for Prone Positioning

Hypoxemic respiratory failure with the following features:

- PaO_2/FiO_2 ratio < 150 despite high PEEP or APRV
- Diffuse bilateral lung infiltrates
- Dorsal consolidation on CT (if available)

Contraindications for Prone Positioning

- **Prohibitive risk of pathogen exposure to ICU staff**
- Unstable cervical spine
- Significant long bone fractures
- Anatomical or treatment considerations that preclude proning

Minimum Necessary Personnel

- 1 respiratory therapist to control the airway and ventilator
- 4 turners (may be RN, MD, PCT, RRT, or student)
- 1 supervisor, who should not be involved in the proning process itself

Turning Process

A. PREPARE the patient

- Apply lubricant to eyes and tape eyelids closed
- Remove any jewelry from the patient's head or neck
- Remove any bite blocks
- Bolus necessary analgesia/sedation/neuromuscular blocker
- Confirm SpO_2 and $ETCO_2$ monitors are in place and functional

B. POSITION the personnel

- Two turners on either side of the patient (four total)
- Respiratory therapist at the head of the patient to manage the head, airway, and face pillow
- If available, one person to manage ventilator tubing and provide backup
- Supervisor at the foot of the bed

C. PAD the patient (if going from SUPINE to PRONE)

- Foam face pillow, making sure the endotracheal tube is not kinked (it may be necessary to cut out some of the foam padding)
- Two pillows each on the chest, lower pelvis, and shins
- Place a sheet over the patient (head to toe) and wrap snugly, bundling the pillows to the patient

D. DISCONNECT (if safe to do so for a brief time)

- Central lines (after necessary boluses)
- Arterial lines
- Hemodialysis lines
- Cardiac monitor leads

F. **TURN the patient—Supervisor should read each step aloud, with verbal confirmation by the team members**

10. Supervisor confirms that the airway and ventilator tubing are under control by the respiratory therapist.

11. Supervisor confirms that all lines and leads have been disconnected (SpO_2 and $ETCO_2$ monitors may be left in place, unless it interferes with the turning process).

12. On the supervisor's count, the team will turn the patient onto his left side, keeping the pillows tight against the body using the sheet.

13. Supervisor confirms that nothing needs to be repositioned.

14. On the supervisor's count, the team will turn the patient to the PRONE or SUPINE position, ensuring that the pillows and face pad are kept in the proper position.

15. Respiratory therapist confirms to the supervisor that the endotracheal tube is at the proper depth and that the tube is not obstructed, with an appropriate $ETCO_2$ waveform.

16. If PRONE, turners confirm to the supervisor that the patient is appropriately padded, and that arms and legs are positioned comfortably.

17. If SUPINE, turners remove padding.

18. Reattach cardiac monitor leads, arterial line, and restart infusions.

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* DO_2 = Cardiac Output × Hemoglobin × SaO_2 × 13.4 + [PaO_2 × 0.003]. As you can see, the vast majority of delivered oxygen is bound to hemoglobin, and so the saturation (SaO_2) is a much bigger component than the dissolved oxygen tension (PaO_2). The contribution of the PaO_2 is so small that that part of the equation is often omitted to make the math easier. So, if a pulse oximeter is well-placed and functioning, frequent ABGs become unnecessary.

* 12.5 grams of 25% albumin IV q6h, with each dose of albumin followed by 20-40 mg of IV furosemide. Alternatively, you could use a furosemide infusion along with the q6h albumin.

Chapter 25

Seven Rules For Severe Respiratory Failure

Positive Pressure Ventilation is supportive, and may be therapeutic, but it is not curative.

Without mechanical ventilation, patients with severe respiratory failure will

undoubtedly die. Positive pressure ventilation can reduce shunt, improve gas exchange, and take over the work of breathing until the patient has recovered. That doesn't mean, however, that the ventilator can do anything to reverse the underlying condition or disease process that has led to respiratory failure.

"It is incident to physicians, I am afraid, beyond all other men, to mistake subsequence for consequence."

—Dr. Samuel Johnson

Don't hurt the patient any more than you have to.

Ventilator-induced lung injury (VILI) has been recognized as a necessary evil since the advent of modern critical care medicine, and to altogether eliminate the risk of any lung injury from the ventilator is not realistic. That said, much VILI is actually an unnecessary evil, since it occurs in the pursuit of "normal" gas exchange or "optimized" physiologic parameters. In cases of severe respiratory failure, the risk of VILI is high and the potential for rewards is small—it isn't reasonable to injure the patient's lungs in order to increase the PaO_2 from 65 to 95, when 65 is sufficient to maintain life. Focusing on doing the minimum intervention necessary to support the patient is much more likely to be helpful in the long run.

"As to diseases, make a habit of two things—to help, or at least, to do no

harm."

—Hippocrates

Throw normal values out the window.

Do what's necessary, not whatever is possible. Chasing the ideal of "normal" gas exchange will inevitably lead to VILI and unnecessary therapeutic interventions, all of which carry very real (and unwanted) side effects. With severe respiratory failure in particular, the twin objectives are to sustain the patient and minimize the risk of further injury. Sustaining the patient is obviously the more important objective, and there will be times when very high ventilator pressures are necessary to achieve it; however, anything that exposes the patient to real or potential harm should be justifiable.

As an aside, this can be the most difficult part of taking care of critically ill patients. We have all been taught what's "normal," and we all face the temptation to do things in order to bring things [lab values, physiologic measurements, vital signs] back into these ranges.

"Striving to better, oft we mar what's well."

—William Shakespeare

Don’t be afraid to experiment….

We use clinical studies and guidelines as a framework for therapy, but what works for one patient may not necessarily work for another. Additionally, the volume of evidence for the critical care of the most severely injured or ill patients is scant. Therefore, it takes a willingness to try different things and an ability to admit when a particular therapy isn’t working. In these cases, protocols and clinical pathways can be harmful in that they can constrain physicians from trying a new approach to the problem.

“If we worked on the assumption that what is accepted as true really is true, then there would be little hope for advance.”

—Orville Wright

… But don’t be afraid to stay the course.

Trying a different approach may be necessary. More often than not, however,

the patient is adequately sustained with his current ventilator settings, but the clinicians are tempted to change course in order to improve the numbers. This has the potential for harm without much benefit and should be avoided. Any modifications should be done either to lower the risk of injury or if the current settings are not providing an acceptable degree of life support. Keep in mind that the medical literature is full of therapies that improve oxygenation, ventilation, and vital signs. Very few of these have actually translated into better patient outcomes.

"Difficulties are just things to overcome, after all."

—Ernest Shackleton

Tracheotomize early.

Patients with severe respiratory failure are in it for the long haul. This means that the chances of improvement in a few days are low and that the need for at least some mechanical ventilator support for several weeks or months is quite high. Couple this with the sedation requirements and relative immobility that accompanies endotracheal intubation, and it's obvious that the sooner the patient has a tracheostomy, the sooner he can begin some degree of mobilization and rehabilitation. A tracheostomy is associated with less sedation, more patient comfort, better mobilization, and fewer days on the ventilator when compared with the endotracheal tube. Do it as soon as it's

safe.

“How poor are they that have not patience? What wound did ever heal but by degrees?”

—William Shakespeare

Remain positive.

Most patients with respiratory failure, even severe ARDS, will eventually recover. Those who survive ARDS will have near-normal lung function after six to twelve months. Even people with cardiopulmonary or neurologic disease who ultimately require a long-term tracheostomy can have an acceptable quality of life. Declaring a patient “ventilator-dependent” or saying that he has “no chance of recovery” after one or two weeks in the ICU may be premature or even wrong. Unbridled optimism isn’t appropriate, but neither is pessimistic nihilism.

Some conditions are not survivable. Some conditions are survivable, and even have the potential for some recovery, but will leave the patient with significant disability and the need for partial or full ventilatory support. Lastly, some conditions are survivable and will require a prolonged period of critical care and ventilatory support, but with a chance at a full recovery to independence. Obviously, nothing is guaranteed, but clinicians caring for

patients with respiratory failure should be able to discern which scenario is most likely and present this to the patient and his family.

Once a treatment plan is decided upon, it is imperative for the clinician to maintain a positive outlook. The patient and his family will be looking for encouragement and guidance, especially when there's a setback or a run of bad days. Throughout the course, the most important thing is open and honest communication. There are times when a shift to palliative care or hospice is appropriate— failure to recover, development of a new and severe complication, or if the patient is unwilling to continue a therapy with a small chance of success that is associated with significant discomfort or an unacceptable quality of life. In these situations, providing the patient and his family with a peaceful, comfortable death is a vital function of the clinician. There may be other times, however, when a setback is temporary and reversible, albeit discouraging (for example, development of pneumonia that requires going back to full ventilator support until it's adequately treated). Here, the clinician should encourage the patient and continue to focus on the ultimate goal of therapy, which is recovery to an acceptable quality of life.

"Takin' on a challenge is a lot like riding a horse. If you're comfortable while you're doin' it, you're probably doin' it wrong."

—Ted Lasso

Chapter 26

Ventilator Flowsheets and Guidelines

These are general guidelines for initial ventilator settings, divided between acute lung injury (sepsis, trauma, ARDS, pulmonary edema, etc.) and obstructive lung disease (asthma, COPD). The specific ventilator management of these patients must be individualized, and the general principles are described in more detail elsewhere in this book. The purpose of these guidelines is to provide a quick reference that is applicable to the majority of patients placed on the ventilator in the ICU or the Emergency Department.

Acute Lung Injury Ventilator Setup
[ARDS, Sepsis, Trauma, Pneumonitis, Pulmonary Edema]

Mode: Assist Control with Decelerating Flow
(aka PRVC, CMV with Autoflow, VC+, etc.)

Tidal Volume: 6 mL/kg PBW
Rate: enough for minute ventilation 6-8 L/min
FiO_2 100%

Set the PEEP

CXR Method

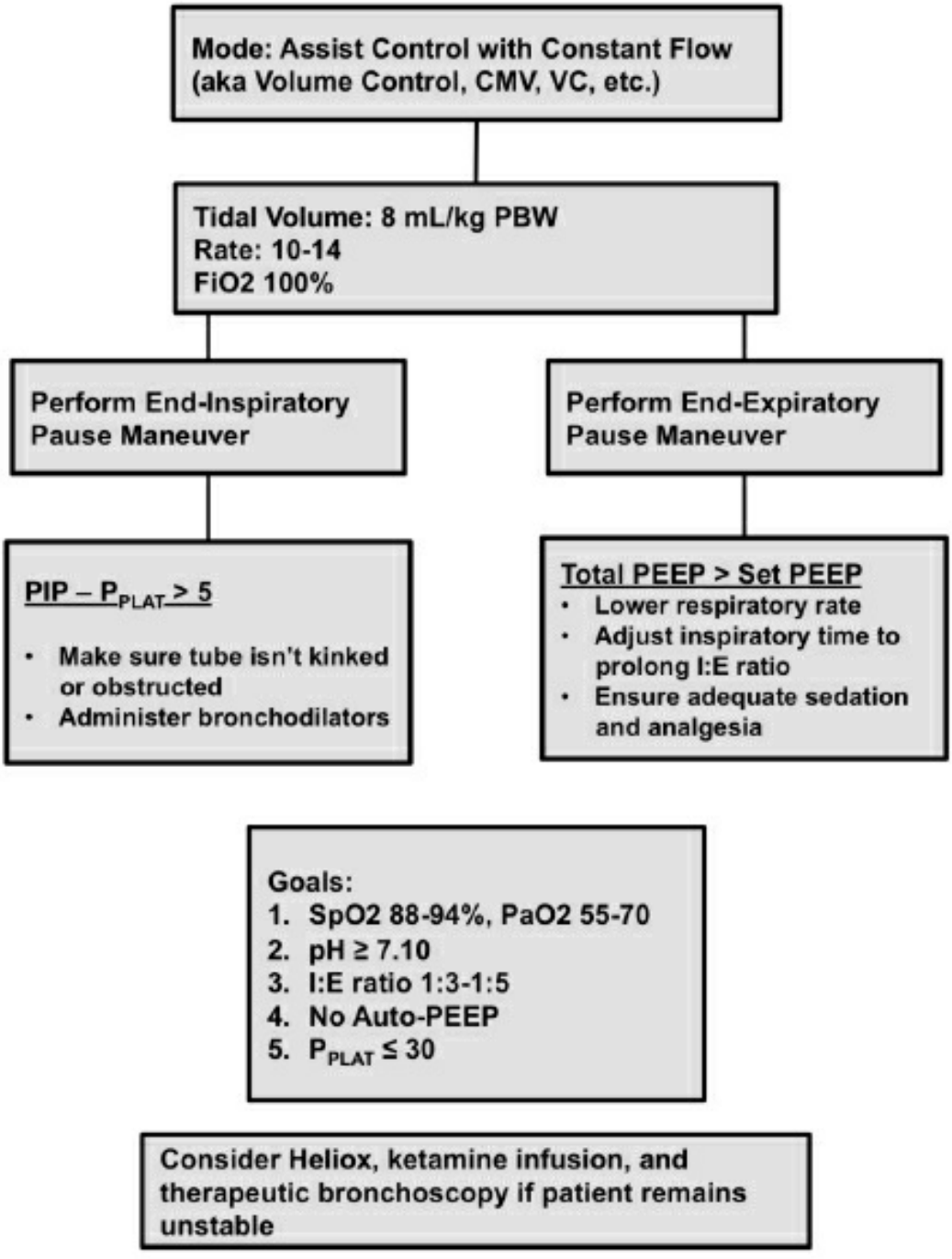
Clear Lungs:	5
Diffuse Infiltrates:	10
Dense Infiltrates:	15
Bilateral White-Out:	20

ABG Method

PaO_2/FiO_2 Ratio	PEEP
201-300	5-10
101-200	10-15
≤ 100	15-20

Goals:
1. SpO2 88-94%, PaO2 55-70
2. pH 7.15-7.45
3. Plateau Pressure ≤ 30

Obstructive Lung Disease Ventilator Setup
[Status Asthmaticus, COPD, Bronchospasm]



Tidal Volume Chart—Females

Height (ft/in)	4 mL/kg PBW	6 mL/kg PBW	8 mL/kg PBW
5’ 0	182	273	364
5’ 1	191	287	382
5’ 2	200	301	401
5’ 3	210	314	419
5’ 4	219	328	438
5’ 5	228	342	456
5’ 6	237	356	474
5’ 7	246	370	493
5’ 8	256	383	511
5’ 9	265	397	530
5’ 10	274	411	548
5’ 11	283	425	566
6’ 0	292	439	585
6’ 1	302	452	603
6’ 2	311	466	622
6’ 3	320	480	640
6’ 4	329	494	658
6’ 5	338	508	677
6’ 6	348	521	695
6’ 7	357	535	714
6’ 8	366	549	732
6’ 9	375	563	750
6’	384	577	769

10			
6’ 11	394	590	787
7’ 0	403	604	806

Tidal Volume Chart—Males

Height (ft/in)	4 mL/kg PBW	6 mL/kg PBW	8 mL/kg PBW
5’ 0	200	300	400
5’ 1	209	314	418
5’ 2	218	328	437
5’ 3	228	341	455
5’ 4	237	355	474
5’ 5	246	369	492
5’ 6	255	383	510
5’ 7	264	397	529
5’ 8	274	410	547
5’ 9	283	424	566
5’ 10	292	438	584
5’ 11	301	452	602
6’ 0	310	466	621
6’ 1	320	479	639
6’ 2	329	493	658
6’ 3	338	507	676
6’ 4	347	521	694
6’ 5	356	535	713

6’ 6	366	548	731
6’ 7	375	562	750
6’ 8	384	576	768
6’ 9	393	590	786
6’ 10	402	604	805
6’ 11	412	617	823
7’ 0	421	631	842

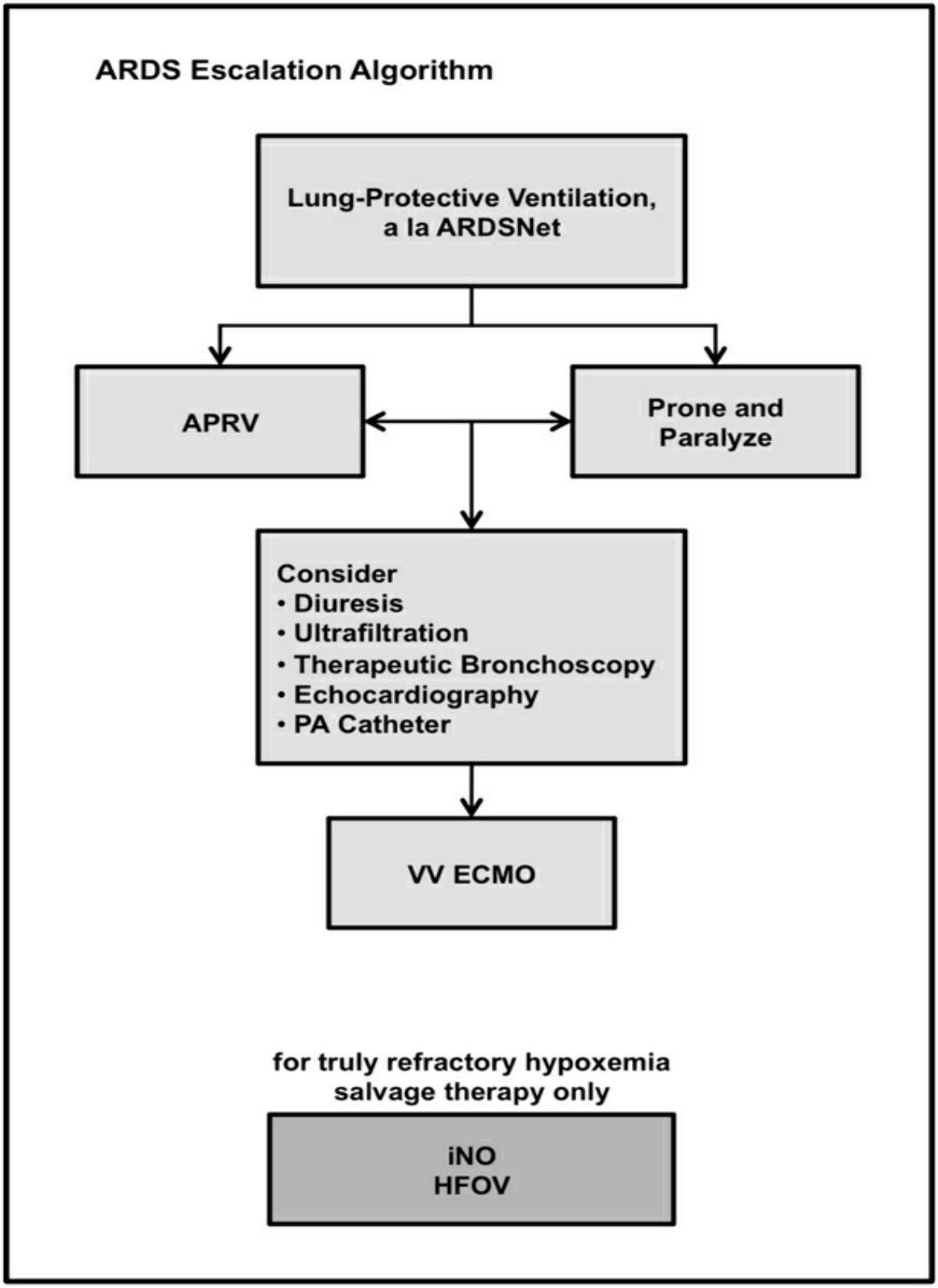
Lower PEEP Table

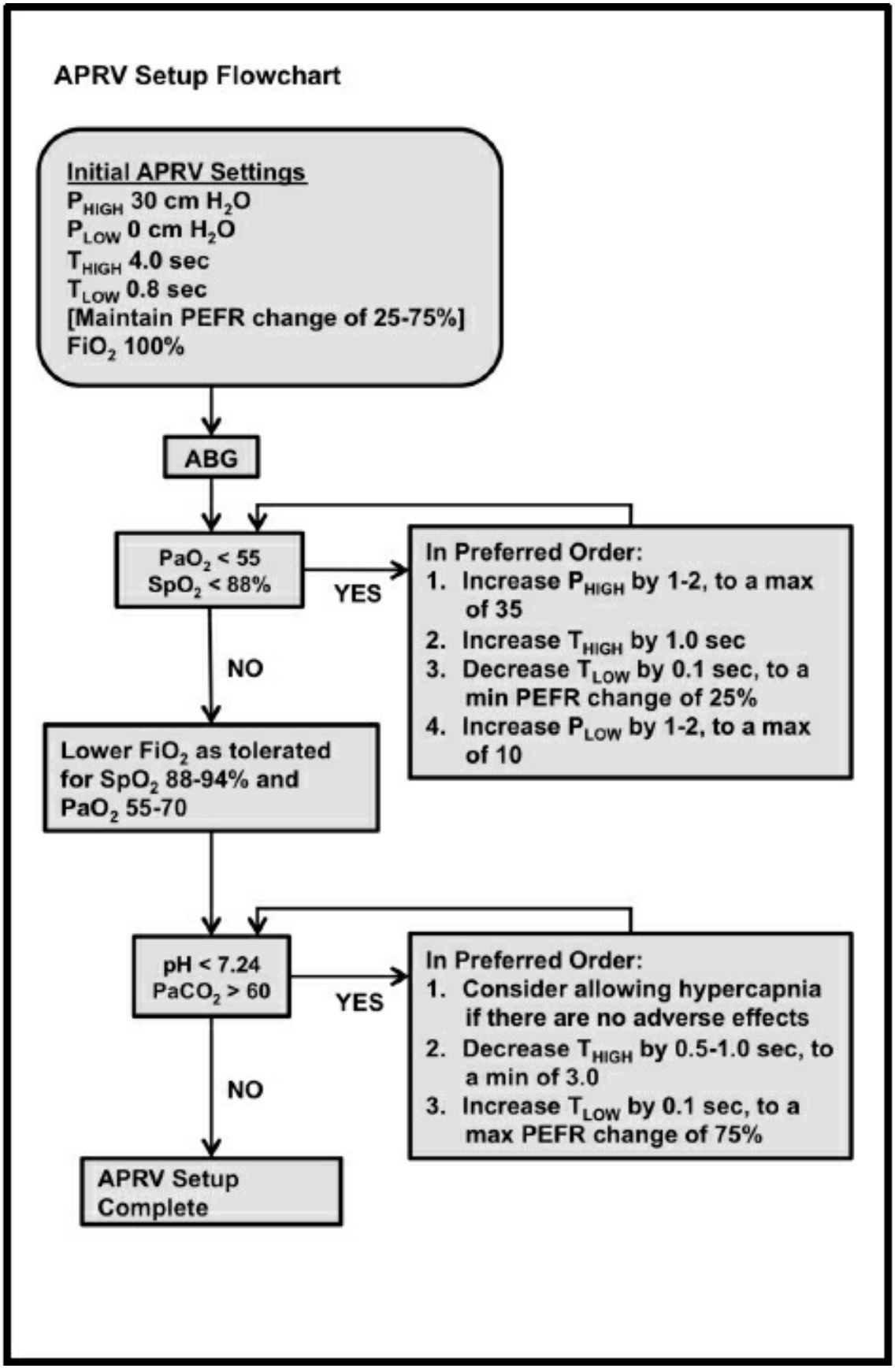
FiO_2	**PEEP**
30%	5
40%	5
40%	8
50%	8
50%	10
60%	10
70%	10
70%	12
70%	14
80%	14
90%	14
90%	16
90%	18
100%	18
100%	20
100%	22

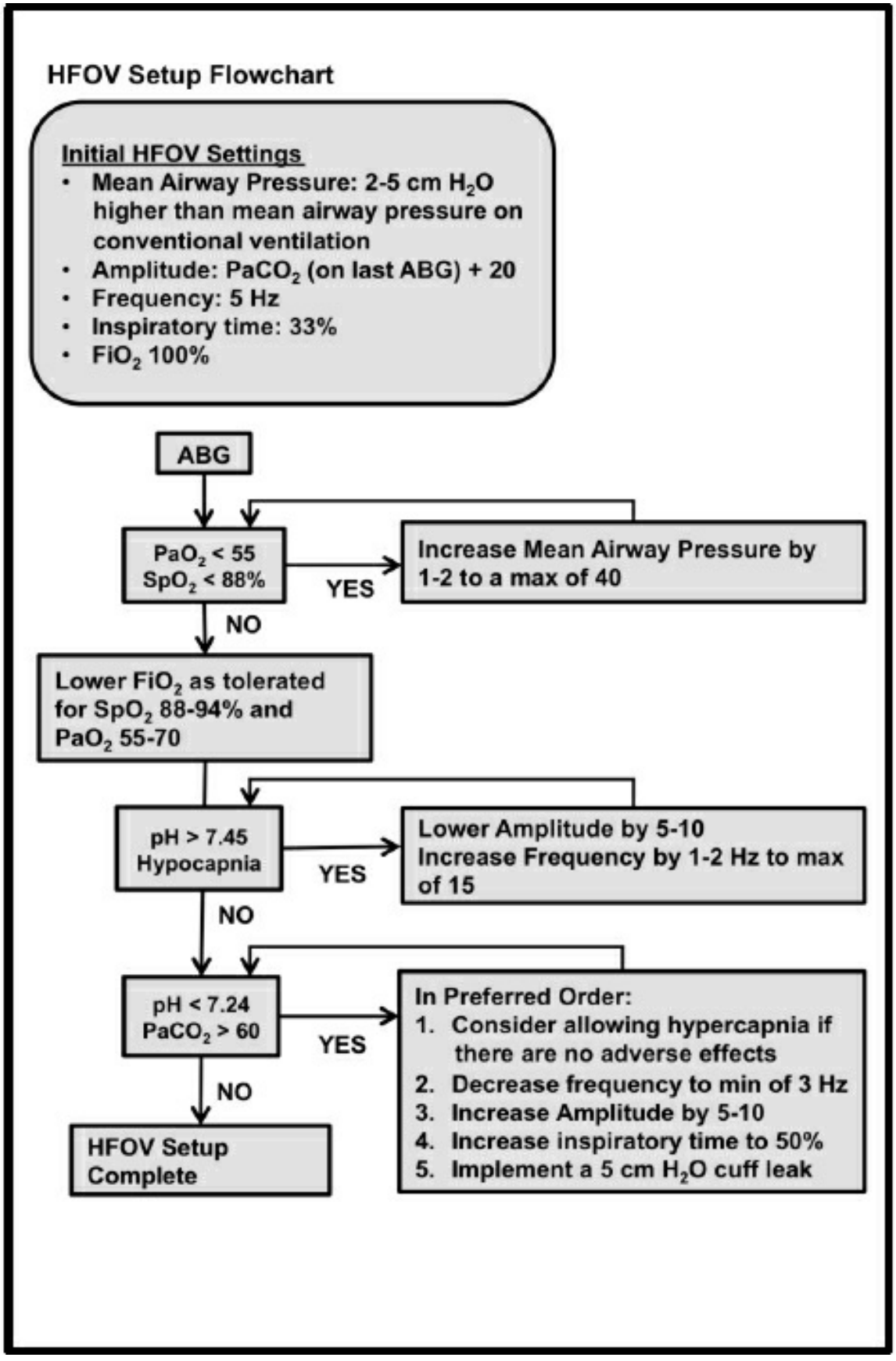
100%	24

Higher PEEP Table

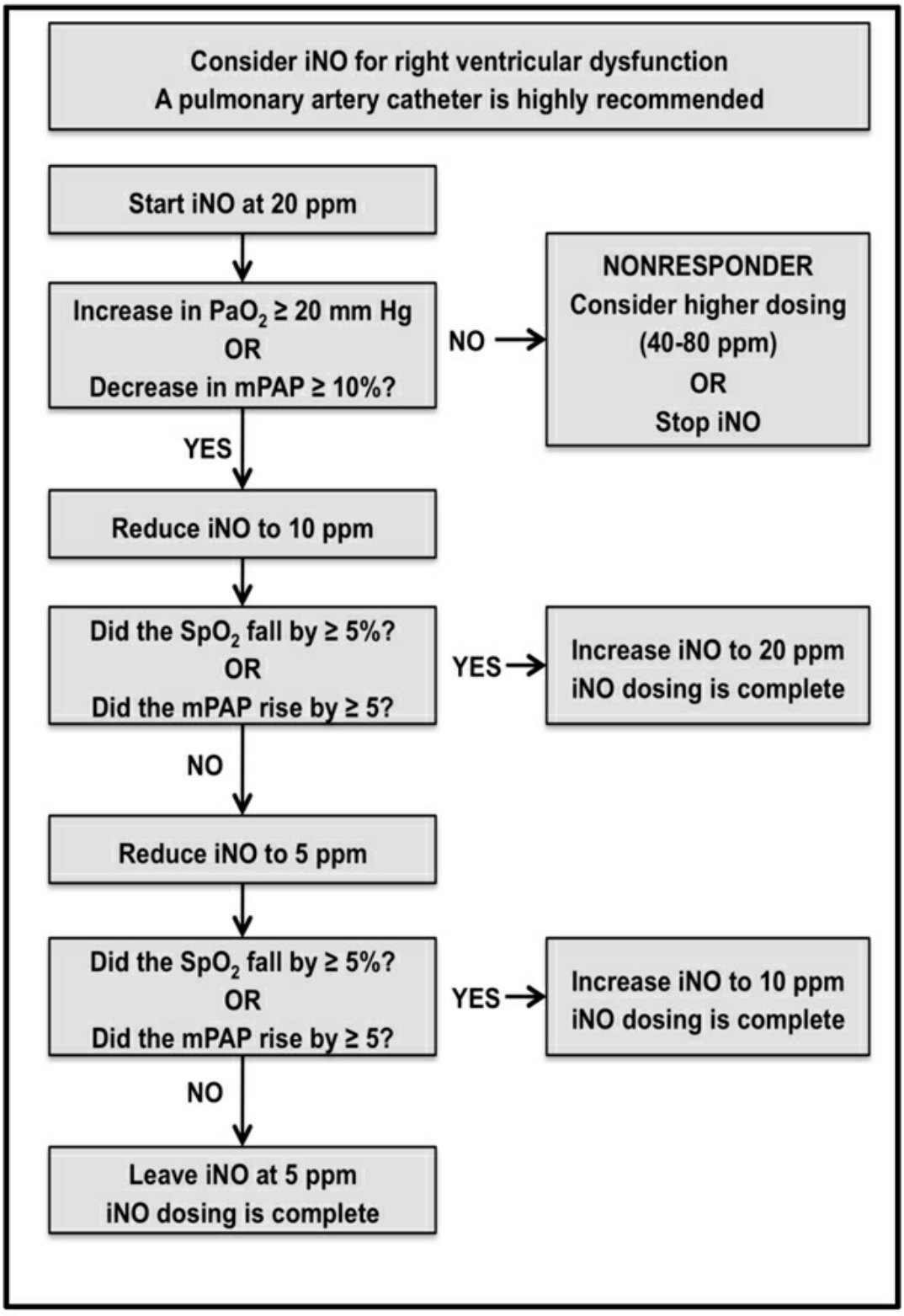
FiO_2	PEEP
30%	5
30%	8
30%	10
30%	12
30%	14
40%	14
40%	16
50%	16
50%	18
50%	20
60%	20
70%	20
80%	20
80%	22
90%	22
100%	22
100%	24


ARDS Escalation Algorithm
Lung-Protective Ventilation, a la ARDSNet
APRV
Prone and Paralyze
Consider
• Diuresis
• Ultrafiltration
• Therapeutic Bronchoscopy
• Echocardiography
• PA Catheter
VV ECMO
for truly refractory hypoxemia salvage therapy only
iNO
HFOV

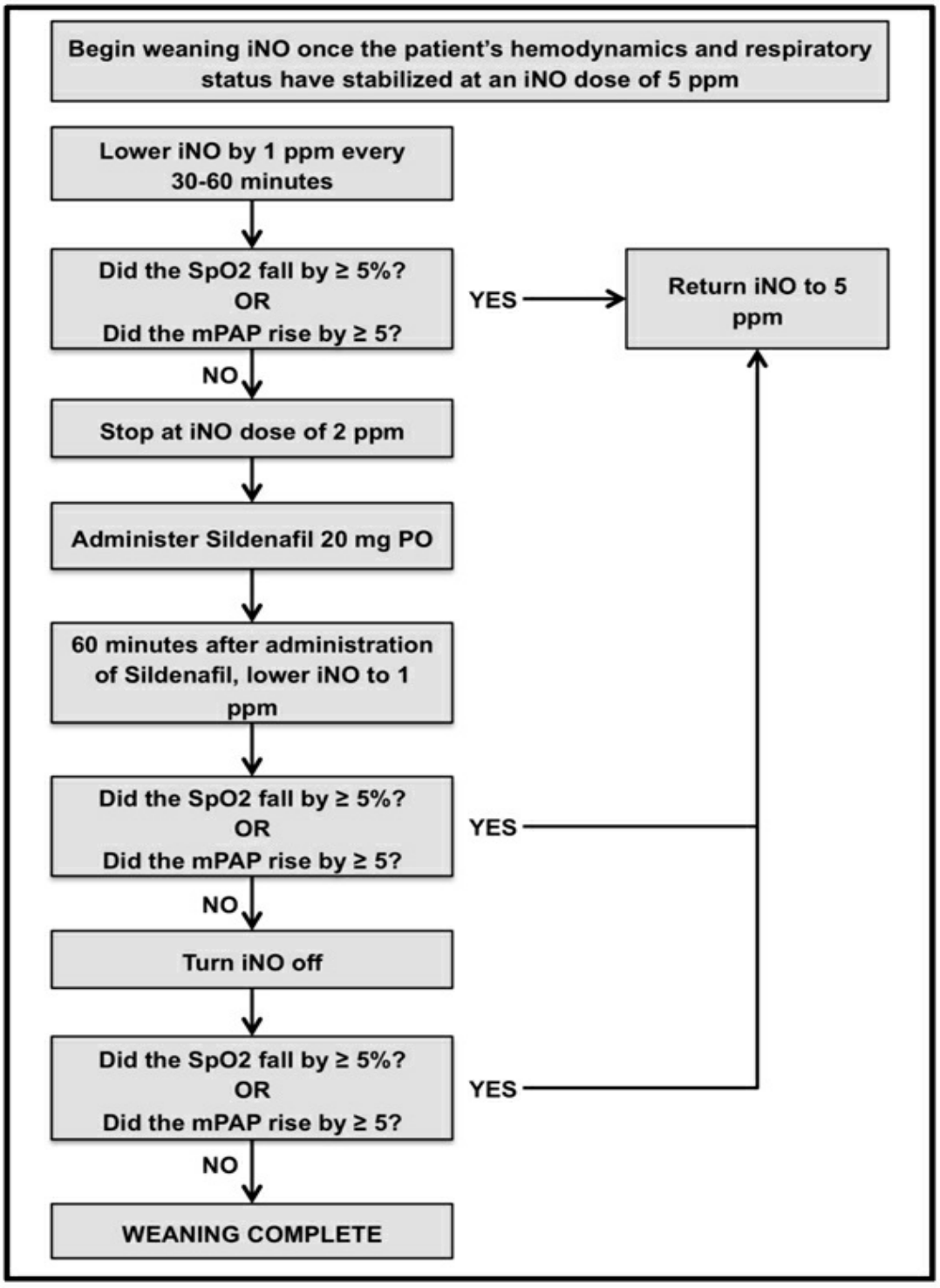

APRV Setup Flowchart
Initial APRV Settings
P_{HIGH} 30 cm H_2O
P_{LOW} 0 cm H_2O
T_{HIGH} 4.0 sec
T_{LOW} 0.8 sec
[Maintain PEFR change of 25-75%]
FiO_2 100%
ABG
PaO_2 < 55
SpO_2 < 88%
YES
In Preferred Order:
1. Increase P_{HIGH} by 1-2, to a max of 35
2. Increase T_{HIGH} by 1.0 sec
3. Decrease T_{LOW} by 0.1 sec, to a min PEFR change of 25%
4. Increase P_{LOW} by 1-2, to a max of 10
NO
Lower FiO_2 as tolerated for SpO_2 88-94% and PaO_2 55-70
pH < 7.24
$PaCO_2$ > 60
YES
In Preferred Order:
1. Consider allowing hypercapnia if there are no adverse effects
2. Decrease T_{HIGH} by 0.5-1.0 sec, to a min of 3.0
3. Increase T_{LOW} by 0.1 sec, to a max PEFR change of 75%
NO
APRV Setup Complete


HFOV Setup Flowchart
Initial HFOV Settings
• Mean Airway Pressure: 2-5 cm H_2O higher than mean airway pressure on conventional ventilation
• Amplitude: $PaCO_2$ (on last ABG) + 20
• Frequency: 5 Hz
• Inspiratory time: 33%
• FiO_2 100%
ABG
PaO_2 < 55
SpO_2 < 88%
YES
Increase Mean Airway Pressure by 1-2 to a max of 40
NO
Lower FiO_2 as tolerated for SpO_2 88-94% and PaO_2 55-70
pH > 7.45
Hypocapnia
YES
Lower Amplitude by 5-10
Increase Frequency by 1-2 Hz to max of 15
NO
pH < 7.24
$PaCO_2$ > 60
YES
In Preferred Order:
1. Consider allowing hypercapnia if there are no adverse effects
2. Decrease frequency to min of 3 Hz
3. Increase Amplitude by 5-10
4. Increase inspiratory time to 50%
5. Implement a 5 cm H_2O cuff leak
NO
HFOV Setup Complete

Initial iNO Dosing Algorithm



iNO Weaning Algorithm



Prone Positioning Checklist*

Indications for Prone Positioning
Hypoxemic respiratory failure with the following features:

- PaO_2/FiO_2 ratio < 150 despite high PEEP or APRV
- Diffuse bilateral lung infiltrates
- Dorsal consolidation on CT (if available)

Contraindications for Prone Positioning

- **Prohibitive risk of pathogen exposure to ICU staff**
- Unstable cervical spine
- Significant long bone fractures
- Anatomical or treatment considerations that preclude proning

Minimum Necessary Personnel

- 1 respiratory therapist to control the airway and ventilator
- 4 turners (may be RN, MD, PCT, RRT, or student)
- 1 supervisor, who should not be involved in the proning process itself

Turning Process

A. PREPARE the patient

- Apply lubricant to eyes and tape eyelids closed
- Remove any jewelry from the patient's head or neck
- Remove any bite blocks
- Bolus necessary analgesia/sedation/neuromuscular blocker
- Confirm SpO_2 and $ETCO_2$ monitors are in place and functional

B. POSITION the personnel

- Two turners on either side of the patient (four total)
- Respiratory therapist at the head of the patient to manage the head, airway, and face pillow
- If available, one person to manage ventilator tubing and provide backup
- Supervisor at the foot of the bed

C. PAD the patient (if going from SUPINE to PRONE)

- Foam face pillow, making sure the endotracheal tube is not kinked (it may be necessary to cut out some of the foam padding)
- Two pillows each on the chest, lower pelvis, and shins
- Place a sheet over the patient (head to toe) and wrap snugly, bundling the pillows to the patient

D. DISCONNECT (if safe to do so for a brief time)

- Central lines (after necessary boluses)
- Arterial lines
- Hemodialysis lines
- Cardiac monitor leads

G. **TURN the patient—Supervisor should read each step aloud, with verbal confirmation by the team members**

19. Supervisor confirms that the airway and ventilator tubing are under control by the respiratory therapist.

20. Supervisor confirms that all lines and leads have been disconnected (SpO_2 and $ETCO_2$ monitors may be left in place, unless it interferes with the turning process).

21. On the supervisor's count, the team will turn the patient onto his left side, keeping the pillows tight against the body using the sheet.

22. Supervisor confirms that nothing needs to be repositioned.

23. On the supervisor's count, the team will turn the patient to the PRONE or SUPINE position, ensuring that the pillows and face

pad are kept in the proper position.

24. Respiratory therapist confirms to the supervisor that the endotracheal tube is at the proper depth and that the tube is not obstructed, with an appropriate $ETCO_2$ waveform.

25. If PRONE, turners confirm to the supervisor that the patient is appropriately padded, and that arms and legs are positioned comfortably.

26. If SUPINE, turners remove padding.

27. Reattach cardiac monitor leads, arterial line, and restart infusions.

Daily SBT Protocol

Assessment Criteria

$FiO_2 \leq 50\%$
PEEP ≤ 8
Able to follow directions
Not requiring frequent suctioning Hemodynamically stable
Not a known difficult airway
Not on unconventional ventilation (APRV, HFOV)
No physician order for "No Daily SBT"

If all of the assessment criteria are met, begin the Spontaneous Breathing Trial

1. CPAP 5 cm, PS 7 cm for 30-60 minutes
2. At the end of the SBT, calculate the RSBI
3. If the RSBI is < 80, extubate the patient
4. If the RSBI is > 80, back to assist-control
5. If there is concern over the patient's readiness for extubation, call the physician

Abort the SBT for any of the following

Desaturation below 88%
Increase in heart rate by 20 beats/min
Significant change in blood pressure
Diaphoresis
Accessory muscle use or paradoxical breathing pattern

SIMV with PS Ventilator Weaning Protocol*

- Assumes patient has a tracheostomy
- Tidal volume 8 mL/kg PBW when on SIMV
- FiO_2 30-50%, PEEP 5-8
- If the patient can't complete the step, return to the vent (if on trach collar) or go back 1-3 steps as needed (if on the vent) and try again the next day

Day	Trach Collar Time	Vent Settings
1	-	Rate 10, PS 20
2	-	Rate 8, PS 20
3	-	Rate 6, PS 20
4	-	Rate 4, PS 20
5	-	Rate 4, PS 18
6	-	Rate 4, PS 16
7	-	Rate 4, PS 14
8	-	Rate 4, PS 12
9	-	Rate 4, PS 10
10	1 hour	Rate 4, PS 10

11	2 hours	Rate 4, PS 10
12	4 hours	Rate 4, PS 10
13	6 hours	Rate 4, PS 10
14	8 hours	Rate 4, PS 10
15	10 hours	Rate 4, PS 10
16	12 hours	Rate 4, PS 10
17	16 hours	Rate 4, PS 10
18	20 hours	Rate 4, PS 10
19	24 hours	-
20	24 hours	-
21	24 hours	-

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[*] Eye and mouth care is essential. Tube feeding in the prone position is permissible if the tube is post-pyloric; otherwise, hold tube feeding while prone and increase the rate of feeding while supine.

[*] Modified from the TIPS Ventilator Weaning Protocol [*Chest* 2001 Jan; 119(1): 236-42.]

Appendix of Useful Formulae

(For board exams, ICU rounds, and to occasionally help an actual patient!)

Alveolar Gas Equation

$P_AO_2 = [(P_B - P_{H2O}) \times FiO_2] - (PaCO_2 / RQ)$

Simplified: $P_AO_2 = 713(FiO_2) - 1.2(PaCO_2)$

Compliance

Δ Volume / Δ Pressure

Normal compliance of the lung: 200 mL/cm H_2O
Normal compliance of the chest wall: 200 mL/cm H_2O
Normal compliance of the respiratory system: 100 mL/cm H_2O

The chest wall and lungs function in a parallel circuit, so the compliance of the respiratory system (C_{RS}) calculated as: $1/C_L + 1/C_{CW} = 1/C_{RS}$

Compliance is a function of body weight, so the normal values listed are for a 75 kg adult. Compliance of the lungs and chest wall is typically 2-2.5 mL/cm H_2O/kg. Compliance of the respiratory system is typically 1-1.25 mL/cm H_2O/kg.

DO_2:VO_2 Ratio

$SaO_2 / (SaO_2 - SvO_2)$

Normal DO_2:VO_2 ratio is 4-5
In critically ill patients, ≥ 3 is acceptable

Driving Pressure (P_L)

$P_L = P_{PLAT} - PEEP$

Elastance

Δ Pressure / Δ Volume

Specific elastance of healthy lung: 13.5 cm H_2O/L

Oxygen Consumption

$VO_2 = (CaO_2 - CvO_2) \times C.O. \times 10$

(CvO_2 is the content of mixed venous blood obtained from a PA catheter, ideally, or else a catheter in the SVC)

Normal VO_2: 200-250 mL O_2/min, or 3 mL O_2/kg/min

Oxygen Content

$CaO_2 = 1.34(Hgb)(SaO_2) + 0.003(PaO_2)$

Normal CaO_2: 20 mL O_2/dL blood

Oxygen Delivery

$DO_2 = CaO_2 \times C.O. \times 10$

(C.O. = cardiac output in L/min)

Normal DO_2: 1000 mL O_2/min, or 12-15 mL O_2/kg/min

Oxygen Extraction Ratio

$O_2ER = VO_2 / DO_2$
Simplified: $O_2ER = (SaO_2 - SvO_2) / (SaO_2)$

Normal O_2ER is 20-25%

Predicted Body Weight

Men: PBW = 0.91 × (Height in cm – 152.4) + 50

Women: PBW = 0.91 × (Height in cm – 152.4) + 45.5

Pulmonary Shunt

$(C_CO_2 – CaO_2) / (C_CO_2 – CvO_2)$

C_CO_2 is the oxygen content of the pulmonary capillary blood. This can't be measured, so the saturation is assumed to be 100% and the P_AO_2 is estimated by the alveolar gas equation. Normal pulmonary shunt: less than 3%

Pulmonary Vascular Resistance

PVR = (mPAP – PAOP) / C.O.

Normal PVR is 2-3 Wood Units, or 160-240 dyne-sec-cm^{-5}

P/F Ratio

PaO_2/FiO_2, with the FiO_2 expressed as a decimal (e.g., 50% oxygen is expressed as 0.50).

A normal P/F ratio is > 500. A P/F ratio < 200 usually indicates a shunt fraction in excess of 20%, which suggests that the patient still needs mechanical ventilation.

Transpulmonary Pressure

The transpulmonary pressure requires an esophageal manometer to estimate pleural pressure.

$P_{TP} = PEEP – P_{ESO}$ (at end-expiration)
$P_{TP} = P_{PLAT} – P_{ESO}$ (at end-inspiration)
This is the driving pressure (P_L)

Typically, the vent should be adjusted to keep the P_{TP} 0-10 at end-expiration, and the P_L 10-15 above the end-expiratory P_{TP}.

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About the Author

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Throughout his career, Dr. Owens has been an active clinician and educator. He enjoys training physicians, nurses, and respiratory therapists in the care of the most seriously ill and injured patients and is a firm subscriber to a holistic approach to critical care medicine. He believes in the rational application of physiology and in always questioning our assumptions.

Dr. Owens lives in Columbia, SC, with his wife and three free-range children. He also lives with a St. Bernard and a beehive with about 60,000 bees. He enjoys mountain biking, whitewater kayaking, playing and coaching lacrosse, and going on family adventures.

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