Under Pressure: “Just Right” is a Moving Target

Rob Graham, R.R.T./N.R.C.P.

I dedicate this column to the late Dr. Andrew (Andy) Shennan, the founder of the perinatal program at Women's College Hospital (now at Sunnybrook Health Sciences Centre). To my teacher, my mentor and the man I owe my career as it is to, thank you. You have earned your place where there are no hospitals and no NICUs, where all the babies do is laugh and giggle and sleep.

“Despite many advancements in the technology behind mechanical ventilators, normal breathing involves negative pressure, and PPV is fundamentally unnatural.”

Ever since mechanical ventilators were first used on babies nearly 60 years ago, the consequences of positive pressure ventilation (PPV) have been apparent. Despite many advancements in the technology behind mechanical ventilators, normal breathing involves negative pressure, and PPV is fundamentally unnatural. Despite the best of intentions and use of lung-protective ventilation strategies, PPV too often results in abnormal pulmonary development with attending long-term sequelae.

While the whole may be greater than the sum of its parts, the failure of one of those parts makes that part the most valuable of all. This is never more so than when the lungs fail. The failure of lungs before they have fully developed presents a veritable quagmire akin to a whack-a-mole game from hell; the fix for one problem creates or is the opposite fix for another.

Pulmonary development is at its infancy (no pun intended) in the sub-25-week post-conceptual age (PCA) baby, and barely able to sustain life, let alone growth at 22 weeks PCA. Be that as it may, Dr. Jonathan Klein of Iowa has shown us that with extreme skill, these infants can and do survive and grow, albeit after a long, costly course in the hospital. Even with the best of care, much of the NICU stay is spent recovering from our efforts to keep them alive.

It is well known that the lungs are most prone to injury during recruitment. While this is true regardless of their stage of develop-

ment, as PCA decreases, the risk of damage and its severity also increase. PPV is the only tool available to us; the only option we have is how we use it. Things get complicated because how much pressure is required to recruit the lung changes depending on what stage of development the lung is in and changes as recruitment ensues. A one size fits all approach simply does not exist.

If critical opening pressure is not reached, recruitment will not occur. The conducting airways must tolerate this pressure without structural compromise during the process. In a mature lung, this is not generally a problem since the airways are robust, but the airways of the extremely premature infant are not well stented or supported and have relatively thin walls. Critical opening pressure may be as much as or more than they can withstand. Alveolar ducts are particularly prone to damage. In the 22-week PCA infant, these are also the portion of the lung most capable of gas exchange at this point; critical opening pressure is their opening pressure and, once reached, must be reduced promptly in order not to induce volutrauma. As PCA increases, there is more lung to recruit downstream of the alveolar ducts, but the ducts themselves remain prone to injury until alveolarization; pulmonary interstitial emphysema likely has its origins in leaking or ruptured alveolar ducts.

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Initial resuscitation is a critical time for the micro-premature infant. Several years ago, changes in the Neonatal Resuscitation Program provided us with oxygen saturation (SpO₂) targets based on time since delivery and initial FiO₂ settings. Before these changes came about, there was a rush to have babies' SpO₂ rise above 90% as quickly as possible and an FiO₂ of 1.0 and PPV with generous peak pressure given. Aside from the neurological consequences of rapid hyperoxygenation in a preterm baby, this rapid transition likely also increased the likelihood of alveolar duct injury. By allowing more time, that the slower transition now NRP dictates, recruitment may be gentler as the extra time may allow

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lower pressure to achieve the same result.

Intubation presents the second (and likely greatest) risk of iatrogenic pulmonary injury even before mechanical ventilation. It is common practice to assess endotracheal tube placement by auscultating manual breaths given via a resuscitation bag. Unfortunately, the pressures used for those breaths are determined mainly by the acuity of the listener's hearing. At this point, the lungs are very likely not fully recruited, and volume is not delivered uniformly; hence, those open areas are potentially subject to barotrauma and volutrauma. The use of a CO₂ detector eliminates the bias associated with auscultation and works with the baby connected to the ventilator. I strongly recommend that before an endotracheal tube is placed, the ventilator should be ready to go with appropriate settings so that the baby can be placed on the ventilator immediately. This preparation gives more precise control of pressure and lessens the risk of damage.

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Volume targeting may be used if available to protect the lungs further. Still, it may provide a false sense of security since a target volume of 4 mL/kg translates to 8 mL/kg if delivered to lungs which are only half recruited. This disconnect is an excellent way to rupture alveolar ducts in an extremely premature baby. Lacking alveoli, extremely premature babies have minimal lung volume to ventilate, and that volume is predominantly composed of the alveolar ducts. I do not believe conventional ventilation modes are suitable for this patient population, and they will not be discussed.

Avoidance of lung injury during resuscitation and recruitment should be the team's primary goal and has the greatest impact on long-term outcomes. Avoid manual ventilation and place a baby on a ventilator using lung-protective ventilation modes and strategies as quickly as possible.

Healthy, recruited, and undamaged lungs require less pressure to ventilate, less PEEP to keep inflated, and are less prone to further damage. The goal of the team in Iowa is to have micro-premature infants on high-frequency jet ventilation (HFJV) by 10 minutes of life; doing so may be why they use low PEEP successfully. It is important to note that PEEP is adjusted to the desired measured PEEP on the jet, not simply dialed in on the conventional ventilator.

Why HFJV? Gas trapping. Tiny babies are very prone to gas trapping, which, in turn, produces hyperinflation. Most of these babies are either hyperinflated or about to become hyperinflated. Avoidance of hyperinflation is key to successful ventilatory management and reducing its effects on not just the lungs but the cardiovascular system as well. There are so many paths to hyperinflation that it might be called the Rome of mechanical ventilation: all roads lead there. The question of how much pressure

is required depends on what is producing hyperinflation. If PEEP (or mean airway pressure (MAP) if oscillating) is not sufficient to maintain airway patency, gas will be trapped distal to any reduction in the airway lumen. As trapped gas accumulates, it presents as hyperinflation on a chest film. In this situation, clinicians may be led to decrease PEEP/MAP, but since insufficient PEEP/MAP created the problem, further reduction increases gas trapping and worsens the hyperinflation. Conversely, too much PEEP/MAP will also create hyperinflation, and decreasing it will decrease or eliminate hyperinflation.

The real problem lies in identifying the root cause of hyperinflation and adapting ventilation to reduce or eliminate that cause. Airway diameter, distending pressure, breath volume, and ventilation rate or frequency are all part of the hyperinflation equation. Small airways have high resistance, which increases time constants and is dependent on adequate distending pressure to maintain airway patency. Larger breath volumes require more time to deliver and even more to exit, and rate or frequency determine how much time is available to accomplish this. Higher rates lead to gas trapping.

How do we know which part or parts of the equation are the problems? Our tests for hyperinflation are very sensitive except lack specificity, but some clues may help. One is PEEP/MAP. The appearance of hyperinflation when PEEP/MAP are relatively low is more likely a result of insufficient pressure than too much but may also be the result of too high a rate or frequency. Decreasing pressure may worsen the problem (and if subsequent CxRs show worsening hyperinflation with a reduction in pressure, it should be increased). Since our goal is to avoid hyperinflation, perhaps the best action in this situation is to reduce the rate or frequency. HFJV rate may be reduced as low as 240 to provide an I:E ratio of 1:12. Reducing frequency in oscillation will provide a more absolute exhalation time but will not change the I:E ratio. On some newer ventilators incorporating HFO modality I:E ratio can be increased to 1:3; however, the increase in amplitude required to deliver the same volume may offset any gains made against gas trapping. Knowing if too much PEEP/MAP is the problem is a more difficult deduction, but if reducing pressure makes the problem worse, it likely is not. Again, here rate reduction is the best course of action.

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If proper action is not taken to mitigate (or preferably eliminate), gas trapping hyperinflation will ensue and progress with malignancy to cystic lungs, extraluminal gas, and pulmonary interstitial emphysema (PIE). Hyperinflation is very difficult to eliminate once established, doubly so if it has progressed to cystic lungs/PIE. Once a veritable death sentence, PIE is best treated with HFJV. Even here, there is debate regarding how much pressure is required. Extraluminal gas accumulation exerts pressure against

the conducting airways, alveolar ducts, and whatever lung has developed distal to them. Without sufficient PEEP/MAP to maintain airway patency and pulmonary recruitment, the result is increased gas trapping, worsening hyperinflation, and finally, complete lung collapse. The “old school” approach to gross hyperinflation and/or PIE was to decrease pressures to allow the lungs to collapse and then re-recruit them. The problem with this approach is in the process, whatever areas of the lungs that are providing gas exchange also collapse. If FiO_2 is already high, it may not be possible to maintain adequate oxygenation in the interim, and atelectasis creates its own problems coined “atelectrauma.” This course of action may be one of the reasons PIE has been associated with such poor outcomes.

With HFJV, we have another tool with which to assess gas trapping: measured PEEP. Measured PEEP displayed on the jet is a very close approximation to tracheal PEEP. This is generally lower than the PEEP value set on the conventional ventilator due to the nature of the jet breath. As measured PEEP on the jet approaches set, PEEP gas trapping is likely occurring, and if it exceeds set PEEP, there is no doubt it is. Measured PEEP reading lower than set PEEP does not necessarily mean gas trapping is not happening since it reflects the average state of affairs and cannot detect regional gas trapping. It is safest to operate on the assumption that tiny babies are gas trapping or soon will be and choose ventilation strategies to mitigate it.

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The severity of hyperinflation is not just gauged by rib counting on a chest film; the ventilation mode makes a difference. When using conventional ventilation (CV) modes, there can be less tolerance of hyperinflation since already inflated lungs must accept relatively large volume breaths with inflating the lungs even more. When uniformly recruited and at distending pressures that maintain the lung in an optimally compliant state, these larger volumes are not as big an issue, although they may still produce shear forces, particularly in the premature infant. The traditional eight ribs of inflation is appropriate here, although even that may be too much for fragile, developing lungs. When a high-frequency ventilation mode is used, a greater degree of hyperinflation may be acceptable since very tiny volumes are imposed on the inflated lungs, and shear forces are significantly reduced. Ten ribs of inflation, in this case, may be acceptable, particularly if the baby is doing well. As they say, the babies do not read the book; if MAP is decreased on a baby with apparent hyperinflation on CXR and they subsequently crump, likely, that baby is not hyperinflated according to their individual physiology. If FiO_2 is low, blood pressure and perfusion are good, the baby may be hyperinflated by

definition, but it is not creating a problem. Of course, this must be monitored closely in order to prevent it from becoming a problem.

Another subset who may tolerate a degree of hyperinflation are those babies with evolving chronic lung disease (CLD). Alveolar simplification, reduced secondary crests, and a thickening of the gas exchange interface are all hallmarks of CLD and lead to a profoundly decreased surface area to support gas exchange and an interface through which gas diffuses with much greater difficulty than in a normal lung. Since CO_2 diffuses 20 times more readily than O_2 , this presents as a relatively easy baby to ventilate but extremely difficult to oxygenate. This is a challenging situation. The lungs are often at least mildly hyperinflated, suggesting a reduction in pressure; however, reducing pressure also reduces diffusion gradient and leads to increased FiO_2 requirements. Here a balance must be struck between hyperinflation and acceptably low FiO_2 . Where that balance lies is a matter of considerable debate. Personally, if cardiac output is good, I am inclined to accept pressure and hyperinflation at the point where FiO_2 is lowest. This represents the compliance “sweet spot” of these lungs.

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A mild to moderate degree of hyperinflation in the face of CLD may actually improve both ventilation and oxygenation in two ways. Because the lungs are stretched, there is an increase in surface area, and the gas exchange interface also thins, and the higher pressure also increases diffusion. This improves overall gas exchange, particularly O_2 , as long as mild to moderate hyperinflation is not allowed to progress to severe hyperinflation. The degree depends on the balance struck by the clinician between oxidative stress and hyperinflation. In my practice, I find many CLD babies do quite well when the lungs are kept at a degree of hyperinflation.

Once severe hyperinflation takes over, options are severely limited. Decreasing MAP may decrease hyperinflation but is just as likely to increase it through increased gas trapping. This will progress to total lung collapse as interstitial gas exerts pressure against parenchymal structures. If total collapse is one's end game, this may be fine (apart from the consequences of total lung collapse).

Another approach may work better and avoid total collapse, i.e., reducing PEEP/MAP and introducing recruitment maneuvers. In this case, they might be referred to as “anti-derecruitment measures.” Imposing low peak inspiratory pressure (PIP) conventional breaths with a long inspiratory time (Ti) may accomplish two things: prevent the collapse of those parts of the lung that are actively contributing to gas exchange while facilitating gas exit

from the lungs by stenting the airways open. I usually start with inspiratory pressure 5 cmH₂O above PEEP or MAP, Ti of 2 seconds, and a rate of 5. MAP may be the same overall, but the way it is delivered changes to give parts of the lung with varying degrees of compliance some time to function at pressure closer to what is optimal for them. Ti may be increased to 3 seconds, PIP may be increased slightly, and the rate may be increased depending on the severity of the situation and resulting effect. In the face of active air leaks, this approach should be avoided or used with extreme caution. Alas, support for this strategy is strictly anecdotal.

“The best way to avoid all of this is to avoid CLD entirely. There is growing evidence to support the intratracheal administration of a surfactant/budesonide preparation in reducing the instance of CLD. (1, 2) Once CLD is established, there may also be some benefit to late or “rescue” surfactant administration. (3)”

The best way to avoid all of this is to avoid CLD entirely. There is growing evidence to support the intratracheal administration of a surfactant/budesonide preparation in reducing the instance of CLD. (1, 2) Once CLD is established, there may also be some benefit to late or “rescue” surfactant administration. (3) Nitric oxide (iNO) with or without late surfactant may also improve ventilation and oxygenation in CLD. (4) Once a naysayer, when it came to late surfactant and/or iNO, I now believe there is a place for both. While metanalysis does not support iNO use in preterm infants, there are theoretical reasons it may help, particularly with pulmonary vascular growth. The cost of iNO combined with the length of time it takes to affect pulmonary vasculature growth, along with the 2011 consensus statement from the NIH, has likely discouraged further investigation. (5) I concur with this reference that further study is warranted. (It is also a good summary of current approaches to CLD treatment). The aforementioned studies suggest that late surfactant/budesonide administration may be even more beneficial; a clinical trial is wanting. (I could find no studies using late surfactant/budesonide).

While I have been discussing invasively ventilated infants, those receiving non-invasive ventilation (NIV) are also “under pressure.” Hereunder is too often the operative word as clinicians may under-support babies leading to extubations failure. When transitioning from an endotracheal tube to NIV, it is essential not to over-wean pressures prior to extubations and provide sufficient support pressure once on NIV. This support should initially be at the level of the last MAP when intubated. Finally, infants should be extubated from pressures that can be reliably maintained using an NIV interface while not creating severe gastric distention.

There is no silver bullet to treat established catastrophic hyperinflation. While the nature of HFJV makes it the best mode in this situation, it takes time and careful management; we can provide

careful management, but we cannot create time. Appropriate pressure and timely response to changing resistance and compliance are vital to avoiding this dilemma or reducing its severity, but they cannot always be avoided.

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In the meantime, we are all under pressure.

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