

Think Small

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.

When it comes to lung protection, less is more.

Disclaimer:

The practices described in this column have evolved with ventilator technology. They are not applicable to the Sensormedics® 3100, which has never been used in Sunnybrook's NICU. High-frequency oscillation, as used with modern, 3rd generation ventilators with integrated HFOV and volume targeting, will not apply directly to American practice until the FDA's full approval of these machines. A history of ventilation at Sunnybrook HSC NICU and how it has evolved into current practices follows.

Post-menstrual age (PMA) notwithstanding, babies are not born with chronic lung disease (CLD). The premature infant is *predisposed* to pulmonary injury, and clinicians worldwide have become quite adept at turning that predisposition into de facto CLD. Dr. Andrew Shennan proposed the definition of CLD as supplemental oxygen required at 36 weeks PMA in the late 1980s (1). While widely adopted, this criterion casts a very large net, and it does not identify the severity of CLD.

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In 2000, a more descriptive definition of CLD was based on how high FiO₂ was and the level of respiratory support required in addition to oxygen supplementation (2). Newer, graded criteria classifying CLD as mild, moderate, or severe are largely based on those proposed in 2000.

CLD, at least the more serious manifestations, has all but disappeared in the ≥30-week PMA cohort. Widespread adoption of non-invasive ventilation (NIV) modes indubitably contributed to the decline of CLD in babies of higher PMA. When it is feasible to use NIV with smaller, less mature infants, it also reduces the risk and/or severity of CLD. It is very important to note that failure to recognise when smaller babies are not tolerating NIV, the risk may increase.

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Many of the improvements in neonatal care (particularly in ventilator technology and ventilatory support) notwithstanding, CLD continues to be ubiquitous in ≤29-week babies. The predisposition to CLD increases with decreasing gestational age at birth, ≈ doubling with each week's decline in PMA. Lower birthweight and having a Y chromosome also pose a higher risk; birthweight <3rd percentile increases the risk of CLD almost six-fold (3). As recently as 2019, reported overall rates of CLD range from 11% – 50%, rising to 20% – 75% when birthweight is <1kg, and ≈80% if born at 22-24 weeks PMA (4). Being able to offer lung-protective invasive ventilation is imperative because it is simply not possible to support extremely premature babies with NIV.

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These statistics need not be a proverbial roadmap to Rome; all roads do not necessarily lead to CLD, even with invasive mechanical ventilation. In previous columns, I have reported CLD rates at the unit I recently retired from, which remain low at $\leq 11\%$. The extremely premature cohort still graduates NICU with a diagnosis of CLD approximately 40% of the time. If the fact that this is half the rate cited in the above data is not remarkable enough, more so is the fact that these babies overwhelmingly share a diagnosis of *mild* CLD, and it is not uncommon for them to be free of supplementary oxygen at discharge. CLD in the ≥ 27 -week PMA is all but non-existent. One might ask, "Where is the road to these outcomes, and how is it found?". I may not be able to answer that question fully, but I may be able to point you in the right direction.

Our patients are small, and with "nano-prems" being successfully resuscitated and admitted to NICU, both their weight and PMA are getting smaller. Small on the outside means small on the inside, and the lungs are no exception. The high resistance characteristic of tiny airways is compounded by their immature, fragile state and structures distal to them. Protecting the pulmonary system from damage secondary to clinical interventions essential for these babies' survival presents a formidable task.

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Before the 3rd generation of microprocessor-controlled ventilators capable of measuring delivered volume, "chest rise" was the metric of positive pressure ventilation. Inspiratory pressures were adjusted to achieve an "adequate" chest rise. "Volutrauma" (5) was neither part of the vernacular nor a concern when discussing lung-protective ventilatory strategies. Barotrauma was the problem of the day, and fear of pressure drove mechanical ventilation practices.

"PEEP-o-phobia" (6) was (and all too often still is) a common manifestation of this fear—inadequate PEEP results in inadequate functional residual capacity (FRC) and sub-optimal lung compliance. Lower pulmonary compliance requires higher inspiratory pressure to deliver sufficient tidal volumes to clear CO_2 and higher FiO_2 to maintain adequate oxygenation. This higher pressure results in conducting airways and alveoli being subject to higher

sheer pressures, increasing the potential for structural damage that can lead to pulmonary interstitial emphysema (PIE). Higher oxygen requirements increase oxidative stress, which leads to abnormal pulmonary development. Today, barotrauma remains a concern. However, most clinicians have learned PEEP is the safest way to provide sufficient mean airway pressure (MAP) and minimise FiO_2 .

Measuring actual tidal volumes in near real-time allows us to adjust parameters to avoid excessive volumes. Some ventilators measure pulmonary compliance in the latter part of the ventilatory cycle and calculate compliance during the final part of inspiration relative to total compliance. This can warn clinicians that they may be over-distending the lung and risking damage. (This is reported as C_{20}/C on the Babylog® family of ventilators.) When displayed graphically, this overdistention is seen as "beaking," a flow/pressure curve change at end-inspiration that looks like a bird's beak (7). This is useful when using conventional ventilation (CV) to help avoid volutrauma but can also provide a false sense of security.

If the lung is not recruited to optimum (or at least adequate) FRC, then the volume delivered to the lung by the ventilator is not evenly distributed. A clinician confident in the thought that they are providing lung-protective ventilation because they are using 4 ml/kg must be reminded that if 50% of the lung has not been recruited, 4ml/kg at the endotracheal tube equates to 8ml/kg delivered to 50% of the lung.

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I very rarely ventilate using CV. When the first generation of ventilators offered integrated high-frequency ventilation (HFOV), the unit at Sunnybrook was the first in Canada to use the mode. It did not take long to realise that most of our smaller babies ended up on HFOV after being ventilated on CV since birth. Since alveolarisation has yet to happen when most babies land in NICU, most of the volume given in CV inflates conducting airways, terminal bronchioles, and alveolar ducts. Air leaks are often the result of tears created by the overdistention of these structures. With this in mind (and in typical cowboy fashion), I started using HFOV immediately in the resuscitation room; it did not take long for everyone else to emulate my practice. It should not have been surprising when CLD rates began to decrease slowly but steadily in these babies.

In those days, virtually all babies with a trachea and an OHIP number (Ontario's premium-free universal public health insurance plan) born at less than 30 weeks PMA were intubated and ventilated. (How loudly they squawked on the admission bed was irrelevant.) Those born at higher PMA were still placed and maintained on CV, yet these babies, by and large, escaped a diagnosis of CLD. Volume measurement was a feature of these ventilators before HFOV became an option, and it was revealed that the volumes delivered to babies using the pressures typical of the day were remarkably large.

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to ventilate, the range of 4-5 mls/kg was deemed more protective. When HFOV became available, 5 mls/kg became an upper volume limit, and 20 cm H₂O was the upper peak inspiratory pressure limit. Babies would be switched to HFOV if these parameters were reached. As with smaller babies, CLD numbers became progressively lower in this “older” and larger cohort. Even before the widespread use of non-invasive modes of ventilatory support (NIV), it was rare for babies of ≥ 27 weeks of PMA to end up with CLD. Today, it is almost unheard of.

Practice involving HFOV also evolved with time. The Sensormedics® 3100A was the only oscillator available to many NICU clinicians before introducing HFOV-integrated machines. The Hummingbird BMO 20N®, a Japanese product, had limited distribution in North America. The Infrasonics Infant Star® (now Nelcor Puritan Bennett®) was ostensibly the first hybrid ventilator. However, its HFOV mode was a flow interrupter, not an actual oscillator. It cannot be directly compared with true sinusoidal wave-producing machines.

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Nonetheless, it earned its place in the hearts of many NICU clinicians. Other high-frequency machines of the time were flow interrupters or had very limited distribution in North America. As with the Bunnell® jet, babies ≤ 25 weeks PMA were not commonly offered resuscitation at the time these machines were being used.

Comparing the Sensormedics® to flow-interrupting devices is an apples-to-oranges affair; comparing it with today's 3rd generation machines is more like comparing apples to concrete. Therein lies part of the problem. As demonstrated by Dr. Jane Pillow, different HFOV machines produce very different results (8). HFOV was considered a rescue therapy at the time (and still is by too many clinicians) and thus was used relatively infrequently and on the sickest babies. HFOV studies had limited subjects to recruit from, and those in the US used the Sensormedics®. That means airway pressure (MAP) was not necessarily adequate, which compounded the problem, as anyone familiar with the “HIFI” oscillation trial of the 1980s can attest to (9).

Anyone who has used the Sensormedics® knows how powerful it is (the “A” model is rated for patients ≤ 35 kg) and that there is no way to measure the volumes delivered. Volumes delivered are assessed by observing “chest wiggle.” As we learned from observing measured tidal volume delivered during CV, chest movement is a very unreliable way to assess volumes. The power the machine is capable of requires frequencies ≥ 10 Hz, 15 Hz being common. Theoretically, if not in actual practice, this increases the propensity for gas trapping. (The machine's rigid circuit makes

positioning difficult and kangaroo care impossible.) The practice of using higher frequencies continued when integrated machines came to market. Since these parameters were most widely used and recommended, clinicians can hardly be faulted for doing so.

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Elimination of CO₂ in HFOV (DCO₂) follows the formula $DCO_2 = f \times Vt^2$ (frequency multiplied by the square of tidal volume); small changes in volume (amplitude (λ)) result in large changes in ventilation. Decreasing f increases volume, and increasing f decreases the volume at a given λ (8). I prefer lower λ to higher, and when f is decreased, I also decrease λ to obtain the same Vt. If there is gas trapping (or if high λ is creating turbulent flow in upper airways), CO₂ may remain the same. Vt decreases as f increases, so a higher λ is required to deliver the same Vt. Increasing f requires higher λ to maintain Vt. Small changes in λ create large changes in DCO₂, and since it is the primary driver of CO₂ clearance, the resulting λ may be lower to maintain the same PaCO₂. Higher λ may necessitate increasing MAP to prevent gas trapping from pinch points or derecruitment resulting from lower trough pressure created by active expiration (10). To avoid this scenario, I practice limiting λ to twice the MAP and monitoring waveform trough pressure.

High λ can produce sheer stress in the upper airways (11). I limit HFOV Vt to a maximum of 2.5, although if λ is low, I will use Vt of 3*. [A quick primary on volume targeted HFOV can be found here (12).] Similarly, I limit λ to 20 cmH₂O, a limit many will consider relatively low. (Many babies will cruise along quite nicely on HFO/VG using λ of less than 10 cmH₂O or delta-P of 10-11 cmH₂O if supported with HFJV.) When either of these conditions occur, it is my (and generally Sunnybrook NICU) practice to change the mode to high-frequency jet ventilation (HFJV). f is generally set at 10 initially and is rarely increased. Instead, f may be decreased to allow lower λ , and Vt may be increased by 0.1-0.3 mls to compensate for the lower minute volume resulting from lower f . These practices align with our philosophy of using lower Vt and pressure. Lower f decreases pressure attenuation and increases the risk of sheer stress (11). However, limiting Vt and λ and changing mode to HFJV early eliminates this risk while reducing the risks associated with gas trapping at higher f .

Perhaps the most contentious issue with both HFOV and HFJV is MAP. Clinicians too often look at a hazy chest film and count ribs to assess lung inflation. In doing so, they fail to appreciate that they are looking at lungs that are not entirely recruited. MAP is

subsequently decreased based on perceived hyperinflation. Derecruitment does not happen immediately upon a MAP decrease, and it is often the next shift that notices climbing FiO_2 ; repeat X-ray all too often is a whiteout.

It must be appreciated that the small volumes used in HFOV, and especially in HFJV, do not create the same sheer stresses produced by the relatively large Vts in CV. This leaves room for more static inflation, without fear of barotrauma or volutrauma produced by the dynamic inflation of CV. Eight ribs may be adequately inflated in CV, but ten ribs (and sometimes more) is acceptable in HFOV/HFJV. If a baby crumps after a drop in MAP, they are telling you that, as far as they are concerned, their inflation is just fine, thank you. Generally, the best inflation results in the lowest FiO_2 and requires the lowest λ to maintain ventilation. To paraphrase James Carville, "It's physiology, stupid!"

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There are factors to consider when using HFOV that influence ventilation. Circuit compliance should be low and without water traps. Water from rainout in the circuit should not be allowed to remain as it will decrease ventilation in HFOV, but may increase ventilation via a superimposed oscillatory waveform when using HFJV. When accumulated in the expiratory limb, it raises MAP (PEEP rises in HFJV, reducing ventilating pressure.) Humidifiers contain compressible volume; they should be small in volume and fill automatically. A low water level will result in a decrease in ventilation.

Thinking small applies to HFJV as well. Here, we use low rates (usually 240, but this can be increased to 300 if nuisance alarms occur) to mitigate gas trapping as much as possible. Permissive hypercapnia is a standard feature of Sunnybrook ventilatory management regardless of the mode used. There is no numerically fixed limit to PaCO_2 provided pH is metabolically compensated to >7.20 . High PaCO_2 has been linked to white matter injury, but PVL is a very rare outcome at Sunnybrook, and our rates of severe intraventricular hemorrhages are not out of line with our comparators.

Think small may be applicable to ventilation, but it is anything but descriptive of the well-coordinated team required to achieve good outcomes. These improvements may not be achieved by cherry-picking one aspect of practice to emulate. While many disagree,

I believe staff (especially respiratory therapists) should be dedicated to the NICU. Aside from being as different from adults as night and day, premature babies are not all the same. Each week of intrauterine development results in changes that make them a different patient. The never-ending NICU learning curve is steep, and NICU clinicians have "...miles to go before we sleep".

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not involved in sales or marketing of the device nor does he receive more than per diem compensation. Also, while the author practices within Sunnybrook H.S.C. This paper should not be construed as Sunnybrook policy per se. This article contains elements considered "off label" as well as maneuvers, which may sometimes be very effective but come with inherent risks. As with any therapy, the risk-benefit ratio must be carefully considered before they are initiated.

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