Ventilation and the Sub Twenty-four Week Micropremie Trying to Hit a Moving Target in the Dark

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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.

Preface:

Of all the controversies over the course of my thirty-year career, the case of twenty-two-week babies and the management (or not) thereof is surely the largest. While one could write endlessly on the ethics surrounding the edge of viability and its definition, I am going to focus on challenging our assumptions about ventilation when we do "go for it."

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This is not meant to serve as a therapeutic guide; rather, it provides food for thought and areas for future research.

Modes:

I believe I can say with certainty NICU's with the best results with the extremely premature (I will refer to them as "microprems") use a high-frequency mode as the first intention. Furthermore, the use of high-frequency jet ventilation (HFJV) is increasing and more likely to be the first intention as well.

The nature of HFJV suits tiny babies best. Issues with a fragile, tiny developing tracheobronchial tree and resulting resistance are greatly reduced. HFJV delivers its breath as a brief puff of gas, which travels more or less down the centre of the airway, much like water going down a drain, the air being at the centre of the rotating water. This allows for concurrent inspiration and expiration, and the swirling nature of the outgoing gas helps mobilise secretions. (1) As endotracheal tube size decreases, effective suctioning becomes virtually impossible. (2)

Tiny airways have very high resistance, and their compliance is high relative to the developing alveolar ducts and primitive alveoli; thus, time constants in these patients are very long. With conventional ventilation (CV), high airway resistance requires high pressures and relatively long inspiratory times (Ti) to deliver a breath. These pressures invariably result in microtears due to airway fragility, while long time constants and high Ti invariably lead to gas trapping; there is not enough time available to both fill the lungs and exhale.

HFJV Ti of 0.02-0.034 seconds significantly mitigates gas trapping, although it can and does still occur. Because I believe gas trapping is the norm in tiny patients, I use low rates (240-300), resulting in generous inspiratory: expiratory (I:E) ratios with "the jet," as long as 1:12. A combination of physics and physiology make HFJV my first choice from the get-go.

High-frequency oscillation (HFO) is often the first mode these babies receive. On larger microprems, this can work and is certainly preferable to any form of conventional ventilation (CV) . The third-generation of oscillators soon to be introduced in the U.S. offer much finer control of HFO than the first-generation thereof. I:E ratio on some machines can be increased to 1:3, and automatic adjustment of breath size gives greater flexibility to the clinician when managing amplitude and breath size. The ability to measure and adjust tidal volume (VT) will be new to American clinicians. Having used these machines in Canada for over 20 years, I can attest to their efficacy, and HFO/VG is used extensively in the unit where I work.

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While there are many advantages to HFO over CV, the nature of HFO renders it less and less efficient as patient size decreases since the HFO waveform is dampened greatly with decreasing airway diameter. The combination of high amplitude and long time constants exacerbates the problem. Increasing I:E to 1:3 give a bit more time for exhalation, but the shortened Ti means higher amplitude must be used to deliver the same volume. Using high amplitude risks creating "choke points" as expiration is active with HFO. Raising mean airway pressure (MAP) to compensate may put undue strain on the cardiovascular system and lungs. In practice, I find decreasing frequency is very helpful; since minute volume is rate multiplied by the square of Vt, a small increase in Vt offsets the drop in frequency. One can thus now deliver more volume using a lower amplitude. HFO adjustments notwithstanding, the result is often unavoidable gas trapping.

Pressures and Volumes:

The magic mean airway pressure (MAP) number to achieve optimal sustained recruitment in practice is usually 10 cmH_2O. One unit starts its microprems on lower pressures with good results. This leads to assumption challenge number one: does the nature of 22-week gestation physiology make 10 cmH_2O too high as an initial setting? HFO requires increasing MAP as amplitude is increased to avoid airway instability and choke points. The unit in

question uses HFJV, which does not share this characteristic with HFO. As a result, perhaps initial PEEP can be decreased when HFJV is the mode of first intention.

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With new oscillators, the target Vt is usually between 1-2 ml/kg. Since airway resistance and Ti are fixed, the only option when delivering a larger Vt is increasing amplitude. While decreasing frequency may help, eventually, ventilation becomes less efficient and requires amplitudes high enough to create choke points. Hence, as HFO Vt approaches that of CV Vt, I am inclined to switch to HFJV. (3) Pressure attenuation with HFJV permits using high pressures to overcome airway resistance without those pressures harming the alveolar ducts, something that clinicians need to be reminded of. There should be no "PIPaphobia" using HFJV. It is not uncommon to use jet pressures of 30 cmH_2O or more. It is also quite common to require delta-pressures of 10cmH_2O or less to maintain acceptable blood gases.

"Normal values":

There is quite simply no frame of reference for normal laboratory values in the microprem, particularly when gestational age is below twenty-three weeks. In practice, we aim for oxygen saturation (SpO_2) of 88-92% and prefer pH no lower than 7.23 while aiming for arterial CO2 ($PaCO_2$) above 40 and below 80 mmHg. In-utero arterial O2 (PaO_2) is approximately 30mmHg while we aim for PaO_2 between 50-80mmHg in microprems and may drop that to 30-50mmHg. (4)

The physiology of the 22-week gestation infant in concert with the nature of O_2 and CO_2 diffusion characteristics makes these targets difficult to achieve safely. In the lung, CO_2 diffuses approximately 20 times more readily than O_2. (5) The microprem lung is in a primitive state of development at 22 weeks gestation, lacking surface area and a functional capillary-alveolar interface. The alveolar duct must serve as the only surface for most diffusion to take place, resulting in huge problems trying to maintain those "normal values." High minute volume and pressure are required to drive O_2 into the pulmonary circulation; however, this results in $PaCO_2$ falling rapidly, especially during initial management when the lungs are still being recruited. Low $PaCO_2$ is a well-known risk factor for intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL). This raises assumption challenges two and three: 2- does low $PaCO_2$ affect the 22-week gestation brain the same way as a more developed one, and 3- have we reached the de-facto limit of what current technology can achieve? (Have we indeed gone too far?)

Given that HFJV is ostensibly the gentlest form of invasive ventilation that we can offer microprems; should we worry less about lower than "ideal" $PaCO_2$ in this patient population when using this mode? How low is safe? In personal practice, these questions have haunted me because I have seen frighteningly low $PaCO_2$ levels. A fourth assumption challenge: are there situations in which low, stable $PaCO_2$ is neuroprotective? A very large patent ductus arteriosus (PDA) can flood the pre-ductal circulation and increase the risk of IVH. Could low $PaCO_2$ mitigate or prevent this? Indomethacin has an initial vasoconstrictive effect followed by reduced cerebral blood flow;6 could low $PaCO_2$ behave similarly? A study out of Calgary confirms the protective effect of indomethacin on IVH, but no definitive association with PDA and IVH was found. (7) There were no infants of less than 23-week gestation in the Calgary study; there is no data on the 22-week gestation infant, and they are not the same as those at 23 weeks. (Shout out to all the physiology geeks out there with animal labs!)

Low PaO_2 levels are a big problem due to the difficulty O_2 has in entering the pulmonary circulation. To achieve "normal" PaO_2 in microprems requires increasing FiO_2, PEEP, or both to facilitate diffusion. The toxic effect of O_2 on the developing infant is well known. Microprems lack antioxidant protection, and the fragile lung will only tolerate so much pressure before air leaks occur, a perfect recipe for chronic lung disease.

Conclusion:

Resuscitation of infants of less than 23 weeks gestation is a new phenomenon. There is a dearth of evidence to guide clinicians in the management of these patients; indeed, this is a de-facto experiment in progress. We have only basic science and physiology to guide us and our expectations, and from which to surmise appropriate therapy. Clinicians may have to operate outside their "comfort zone" if they are to be successful, providing success is a possibility.

References:

1. *Ti of 0.02-0.034 seconds means the vast majority of expiration is passive, and due to lung recoil.*
2. *There is no suction catheter available that will pass down a 2.0 ETT, and the high resistance of even a 6 Fr catheter limits its efficacy.*
3. *I use CV Vt of 3-4 ml/kg with microprems and rarely exceed 3 ml/kg using HFO.*
4. *https://uichildrens.org/health-library/comments-oxygen-toxicity-and-retinopathy-rop-premature-infant*
5. *https://teachmephysiology.com/respiratory-system/gas-exchange/gas-exchange/*

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6. https://www.jpeds.com/article/S0022-3476(13)00118-2/abstract
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