Respiratory Care and its Impact on Neurodevelopmental Outcomes: What's Good, What's Bad, and How Can We Do Better

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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.

That respiratory outcomes impact other outcomes is well known; significant respiratory disease often is linked with other morbidities. What we do as respiratory clinicians is obviously front and centre when it comes to respiratory outcomes, whether chronic lung disease (CLD) or pulmonary function later in life. When it comes to neurodevelopmental outcomes (NDO), the link to respiratory care is less widely known. This may be due to a lack of strong evidence or the perception of some neurodevelopmental practices as "soft science," however, just as the knee bone is connected to the thigh bone, respiratory care plays a part in neurodevelopment and outcomes thereof.

When I started my NICU career some 30 years ago, the Newborn Individualized Developmental Care and Assessment Program (NIDCAP) was being initiated in the Women's College Hospital NICU (now at Sunnybrook Health Sciences Centre). NIDCAP was frowned upon then as the epitome of "soft science," dare I say thrown into the "granola pile" of wishy-washy concepts. Fortunately, times have changed, and that "wishy-washy" concept has been widely adapted into the realm of NICU care. It has brought us to view what we do in terms of medical intervention through a developmental lens. As such, it has also forced a reevaluation of how we do what we do and when we do it. In a sense, we have begun to learn the non-verbal language of premature babies, the cues they give us.

Intubation:

Endotracheal intubation under rapid sequence induction (RSI) should now be a standard of practice for both developmental and physiological reasons. What medication(s) are used may be subject to debate and study, but the concept of pain management and regulation of cerebral blood flow should not be part of that debate. Given the high risk of intraventricular hemorrhage associated with the first seventy-two hours of life, RSI is especially important during resuscitation. Every effort should be made to support the baby non-invasively until vascular access is obtained unless the baby is apneic and bradycardic despite resuscitative efforts.

The placement of an endotracheal tube (ETT) may influence outcomes. Nasal intubation has always been routine in the unit in which I practice. Since very few NICU's nasally intubate, finding evidence to justify this practice is rather difficult as evidence is either non-existent or sparse. From a philosophical standpoint, one can, I believe, make a case for it except in emergent situations. Even in those cases, a clinician skilled at nasal intubation can place an ETT nasally as deftly as orally, if not more so, with most babies.

As a general rule, what goes into a premature baby's mouth should feel good and taste good. We know that infants are orally fixated, and it follows that premature infants would be as well. Oral aversions are a huge obstacle to establishing proper feeding and discharge home, not to mention the costs associated with gavage feeding or more invasive interventions. Self-soothing is also more challenging when an orally placed ETT is taking up most of the oral cavity, leaving little room for a pacifier.

In my experience, nasally placed ETT's are more easily secured and stabilized than oral ones: they are less prone to inadvertent movement and are less affected by oral secretions. This may result in less tube re-taping and fewer unplanned extubations. In turn, the risks associated with repeated intubations such as tracheal stenosis and thus the need for tracheostomy or corrective surgery are reduced. These complications are nigh to non-existent in our NICU. It is my practice to offer sucrose to a baby undergoing an ETT re-taping, in conjunction with comfort measures such as hand hugging provided by a second caregiver. Anything that reduces an infant's stress level is a good thing.

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Ventilation:

Many factors muddy the waters when examining the evidence supporting one mode of ventilation over the other, be it for reducing chronic lung disease (CLD) or providing neuroprotection. Different machines and variation in clinical practice, even within the realm of a study, make it hard to compare apples to apples, or apples to onions as it were. Be that as it may, there are ventilatory practices that we have a pretty good idea affect outcomes adversely.

That CO_2 plays a role in cerebral blood flow, and intraventricular hemorrhage (IVH) is well known, but the relationship may be more complicated than a simple set of values. Since CO_2 has a direct effect on cerebral vasculature tone, it is easy to point to it as the culprit when IVH occurs. Certainly, very low levels are bad, as are very high levels. What, exactly, those levels are is somewhat nebulous. Some studies link high levels to white matter injury, and it is well accepted that levels ≤ 30 mm Hg are to be avoided at all costs. Equally important is the avoidance of rapid changes in CO_2 levels; the body prefers stasis. Many have a "knee-jerk" reaction when they see either very high or very low CO_2 levels and adjust ventilation too rapidly to what is acceptable for the patient. This may create reperfusion injury as vasculature rapidly dilates or constricts, similar to the effects of swings in serum oxygen levels. It is better to make slower adjustments, which allow a more gradual change in vascular tone to avoid this type of scenario unless, of course, pH is life-threatening.

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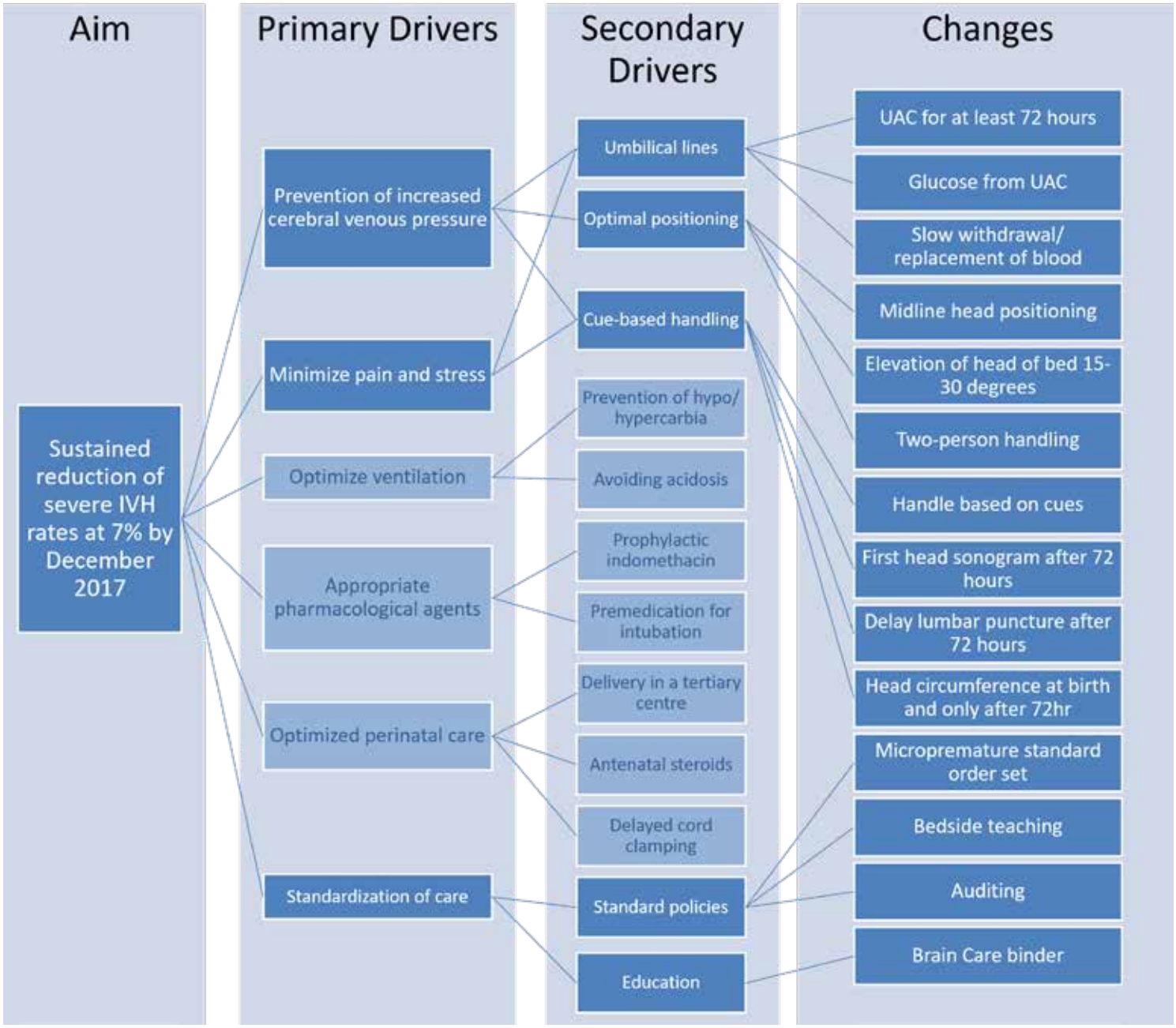
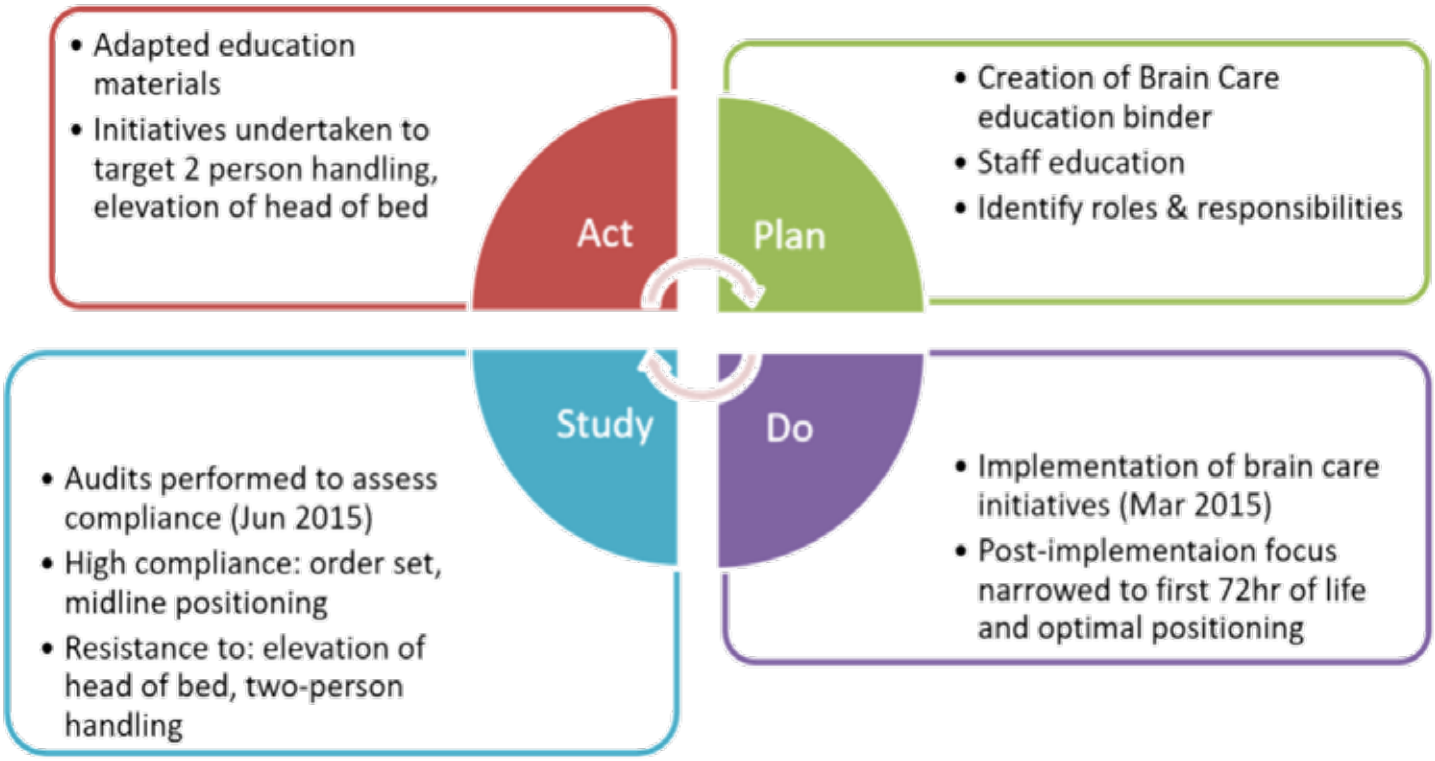
controversy for a very long time. It is accepted that moderate hypercapnia can reduce lung injury, but there are variations in clinical practice as to how much hypercapnia is acceptable. In my practice, relatively high levels of hypercapnia (70-90 mmHg) are tolerated, provided pH is compensated, and the baby is well into their NICU stay. This does not appear to have influenced our rates of IVH or periventricular leukomalacia (PVL).

Acceptance of hypercapnia in the initial 72 hours of life is not advisable in the premature infant already at high risk of IVH. Unfortunately, determining what a baby's CO_2 is during the first hour or so of life can be very difficult since transcutaneous monitoring is very unreliable with low perfusion. Vascular access is time-consuming and active resuscitative measures make capillary sampling impractical, not to mention blood gas turnaround time that may exceed thirty minutes. Much can happen in this time since as the lung is recruited; ventilation improves dramatically. It is my strong belief that paediatric societies and the Neonatal Resuscitation



The concept of "permissive hypercapnia" has been a subject of



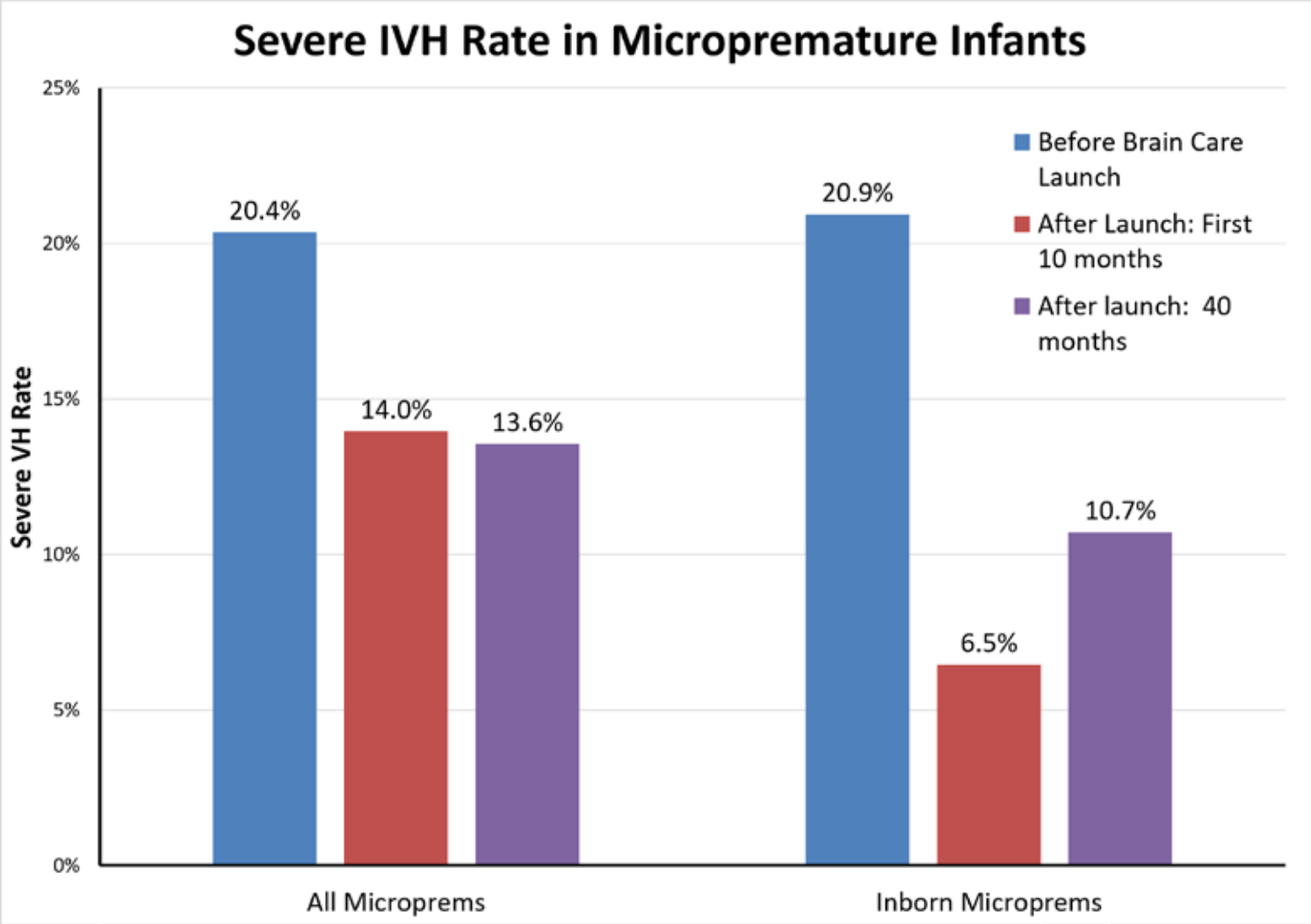
Program should mandate the availability of point of care testing for blood gas analysis in every resuscitation room.

When it comes to modes of ventilation, establishing the superiority of one over another involves so many variables as to make it almost impossible. Having said that, there are some existing studies that provide food for thought. A British study showed significant differences in pulmonary function tests at age 11-14 in premature infants supported with HFO c.f. conventional ventilation (CV), and educational attainment also favoured the HFO group. Emotional issues were greater in the HFO group but were not supported by parent or teacher observations. (1) While a French study initially showed increased IVH with HFO, later analysis showed increased mild IVH but decreased severe IVH and less cerebral palsy in the same group. This is in line with a meta-analysis of IVH and high-frequency ventilation, which showed no increase in the incidence of IVH or PVL with HFO once the results of the disastrous "HIFI" trial of the early 1980s were excluded. (2) Thus it would appear HFO/HFJV ventilation is at least as safe as CV and may result in better long-term developmental outcomes. The caveat with HFO/HFJV ventilation is one must be vigilant regarding CO_2 levels as both modes are capable of dropping CO_2 very quickly, especially when first initiated. Again, point of care testing for blood gases should reduce inadvertent alkalosis/hypocapnia. There is evidence to support HFO over CV, and also evidence suggesting the use of synchronized intermittent mandatory ventilation plus pressure support (SIMV/PS) should be avoided. (3)

The increased utilisation of non-invasive ventilation (both CV and HFO) may be helpful in reducing CLD; however clinicians must recognize that high FiO_2 for prolonged periods of time is detrimental to long-term pulmonary function, and if pressures are not adequate to provide proper functional residual capacity (FRC) there is no benefit to this approach and, as suggested by the HIFI study, may be detrimental. (4)

Positioning, handling and interventions

A quality improvement project in the unit in which I am employed concentrated on reducing severe IVH. Among the changes involved was positioning of the head, and raising the head of the bed to 15 to 30 degrees. Also included were the routine placement



of umbilical lines, minimal, cue-based handling, and 2-person handling. Limiting handling during the first 72 hours is critical; placement of umbilical lines minimizes any disturbances to the baby associated with blood sampling, and the second person involved with 2-person handling provides comfort to the baby (hand hugging, etc) during necessary interventions. The results are shown below (with apologies for the quality of the images).

Clearly outcomes can be improved, and a reduction of severe IVH bodes well for longer-term developmental outcomes.

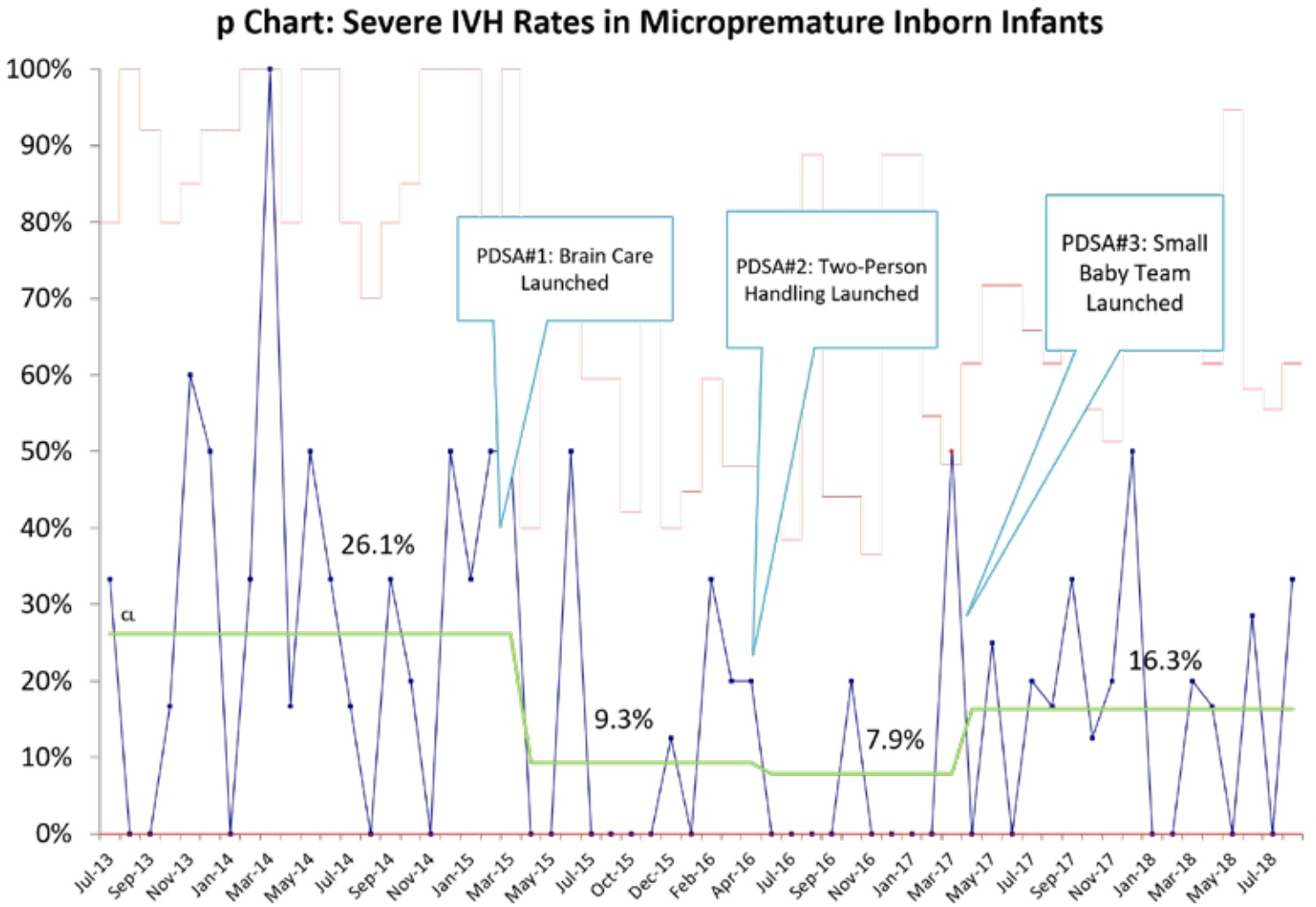
Parental interaction/Kangaroo care (KC)

The link between neurodevelopment and parental interaction with their child has been slow to establish; however there is now evidence to support direct parental involvement in the care of their child in the NICU. The concept of parents as a nuisance, to and in the way of, routine care is being replaced with the reality of parents being an essential part of that care and a positive influence on outcomes, although barriers to its implementation remain among care givers. (5) Respiratory clinicians can actually be one of the greatest enablers of KC; they can also be the greatest obstacles. Concerns regarding ETT stability and extubations are well-founded but can be mitigated, and the benefits, in my opinion, outweigh the risks.

KC was first used as an adjunct to temperature regulation and has been shown to be beneficial in that regard. It is now known that KC affords much more than thermoregulation, it changes the way the premature infant's brain wires itself. Benefits include earlier establishment of breast feeding, (6) improved cognitive and behavioural performance even after 20 years, (7) decreased nosocomial infections, and increased survival.(8)

Kangaroo care may be offered to ventilated infants and is a routine event in the NICU at Sunnybrook, even for babies on HFJV. Care must be taken to avoid the risk of inadvertent extubations.

Supporting evidence for "cycling" infants on NIV, particularly NC-



PAP, is lacking. One of the reasons for this is that studies tend to examine the length of stay or days on respiratory support as a primary outcome. While this is, of course, an important factor for a multitude of reasons, there are "softer" outcomes that may be of importance. One of these is the barrier ventilatory support has on the likelihood of being offered or accepting KC. As well, I believe there is a positive psychological effect on parents when they are able to KC their baby without the cumbersome CPAP apparatus getting in the way, and the challenges associated with maintaining proper pressures while doing so are no longer a factor. In my experience, this practice does not have any adverse effects on infants; providing selection criteria is appropriate, i.e., minimal FiO_2 and supporting pressure. I suspect that should the duration of positive pressure ventilation, and parental comfort/anxiety were added to outcome measures, the findings would be favourable.

Conclusion

While ventilation strategies in the NICU remain varied and controversial, the evidence does provide a link to neurodevelopmental outcomes and respiratory support as well as adjunctive measures improving those outcomes. To quote Robert Frost," we have long to go before we sleep."

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