

new programs, and 5) absence of such cases missed in primary TSH screening programs...⁸ A study to determine the value of routine second specimen testing is underway, sponsored by the US Health and Human Services Secretary's Advisory Committee on Heritable Disorders in Newborns and Children. (H. Hannon, Centers for Disease Control, personal communication). In the meantime, if routine second screening does not become more widespread, it will not be possible for the Colorado algorithm for CF screening to be taken up widely, although it should probably be adopted by all states that currently collect a second sample. The method of looking at new approaches by carefully dissecting retrospective data is to be commended, and this approach has wide applicability to all screening programs. ■

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Automated Adjustment of Oxygen in Ventilated Preterm Infants: Turn on, Tune in, ROP out?

The death of newborns from respiratory failure has been recognized and noted to occur more frequently in preterm infants for >2000 years.¹ In the mid 20th century, the term respiratory distress syndrome (RDS) was coined to describe the often lethal respiratory distress and episodic apnoea, cyanosis, and bradycardia seen in preterm newborns, which began at or shortly after birth and progressed over 72 hours. Hyaline membrane disease (HMD) described the striking pathological features seen on post-mortem examination of lung tissue of infants who died.

Illustrating doctors' enduring enthusiasm for introducing new and unproven therapies, oxygen was first given to newborns in 1780, within 6 years of its discovery.¹ Oxygen supplementation for newborns began in earnest in the 1940s. Although oxygen given in high concentrations likely improved survival from RDS, it resulted in an epidemic of blindness caused by retinopathy of prematurity, thereby starting modern-day neonatologists' ambivalent affair with oxygen.² In an attempt to prevent blindness, oxygen use was curtailed, which led to an increase in deaths from HMD and was associated with a rise in the frequency of spas-

tic diplegia.² Therapy for RDS has progressed markedly in the last 60 years. The introduction of mechanical ventilation was met initially with limited success initially and, with the emergence of bronchopulmonary dysplasia, which was attributed partly to excessive oxygen exposure.³ Continuous positive airways pressure showed an impressive reduction in mortality in a small case series of infants with established severe RDS.⁴ Antenatal steroids were demonstrated to reduce the frequency of RDS and death in preterm infants.⁵ Techniques of mechanical ventilation, which included the use of positive end-expiratory pressure, were refined, and exogenous surfactant therapy followed, resulting in immature infants surviving in greater numbers.⁶ These survivors, however, had substantial rates of chronic lung disease (CLD) and neurological dysfunction. Vitamin A supplementation⁷ and caffeine therapy⁸ were subsequently demonstrated (modestly and substantially, respectively) to reduce the rate of chronic lung disease. Despite showing promise in cohort studies, use of nasal continuous positive airways pressure in preference to endotracheal ventilation from birth did not reduce the rate of CLD in a recently reported randomized trial.⁹

Although the fraction of inspired oxygen (FiO₂) given to infants with respiratory distress was once determined with clinical assessment of color, in time this was aided and

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CLD	Chronic lung disease
FiO ₂	Fraction of inspired oxygen
HMD	Hyaline membrane disease
RDS	Respiratory distress syndrome
SpO ₂	Oxygen saturation

usurped by intermittent measurement of oxygen tension in arterial blood, and subsequently by continuous oxygen saturation (SpO₂) monitoring. We now monitor the oxygen levels of our smallest patients more closely than before, and the rate of visual impairment in survivors has fallen with time. Despite this, many survivors still have chronic pulmonary dysfunction and, more concerning, neurodevelopmental impairment. Cohort studies have shown associations between higher SpO₂ targets and poorer visual and pulmonary outcomes in premature infants.¹⁰ A randomized trial showed that targeting higher SpO₂ in preterm infants who remained receiving oxygen at 32 weeks resulted in worse pulmonary outcomes (prolonged oxygen therapy, higher rates of CLD and home oxygen therapy).¹¹ The “optimum level of oxygenation (to balance 4 competing risks: mortality, retinopathy of prematurity blindness, chronic lung disease, and brain damage)...remains unknown,”² and several large trials comparing relatively lower and higher SpO₂ target ranges for preterm infants are ongoing. Although it is not yet known which is preferable, 3 things are clear: the optimal range is likely lower than many that were previously targeted, there is widespread interest in maintaining infants SpO₂ within predefined ranges, and maintaining infants within these ranges is often difficult.

In this issue of *The Journal*, Claire et al report the results of their randomized crossover trial comparing the ability of a computer system that automatically adjusts FiO₂ to that of a bedside nurse manually adjusting the FiO₂ in keeping the SpO₂ of ventilated infants within a target range.¹² The 16 extremely preterm infants they studied had been ventilated for a mean of 4 weeks and were receiving a mean of 32% oxygen at the time of enrollment. Infants were studied for 8 hours, 4 hours of automated FiO₂ control and 4 hours during which the bedside nurse adjusted the FiO₂. They found that infants had shorter periods outside the target SpO₂ range during automated FiO₂ control. In particular, they had shorter periods of SpO₂ > 95% and ≥98%. Infants spent more time with SpO₂ < 88%, but not <85%. Also, the nurses made fewer manual FiO₂ adjustments during the automated period. The authors are to be commended on their well-designed and executed study. Although the number of infants enrolled is small, the crossover design of the study strengthens its findings. Although some readers might be disappointed that automated FiO₂ control did not maintain SpO₂ exclusively within the target range, it would be unreasonable to expect this of such a strategy, because chronically ventilated infants have falls in SpO₂ for reasons that are not amenable to correction by adjusting FiO₂ alone (eg, forceful expiration against the ventilator with loss of residual lung volume).

Should we all rush out to buy this technology to use in the nursery today? In my opinion, no. Although this novel technology might spare 2 treasured resources in any nursery—the time and sanity of the bedside nurses—we don’t yet know whether it helps the babies. Whether it results in tangible benefits for preterm infants can only be adequately addressed in the context of a well-designed randomized trial

of sufficient size and power to detect meaningful differences in clinically important outcomes. The focus on oxygen and its potential for causing harm in infants has now retreated to the first minutes of life. Randomized trials have demonstrated that air is as effective as 100% oxygen for resuscitation of asphyxiated term infants and is associated with lower mortality.¹³ Although the experience of using <100% oxygen in preterm infants at birth is limited, lower concentrations have been advocated¹⁴ because preterm infants have limited anti-oxidant defenses and a large oxygen load early in life could trigger inflammatory changes that induce end-organ damage. It would be intriguing to see whether automated FiO₂ control would benefit not only the chronically ventilated and oxygen-dependent infants Claire et al describe (who, although infrequent, seem ever-present), but also whether using this approach earlier rather than later might reduce the number of extremely preterm infants reaching this state. ■

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Internal Versus External Influences on Energy Intake: Are Disinhibited Eaters Born or Created?

Parents of obese children often describe the child as “always hungry” or that he or she “doesn’t know when to stop eating,” with the implication that there is something awry in the child’s brain or metabolism. The biological conundrum for clinicians is whether such children do indeed have inherently different appetite and satiety signaling, but the practical challenge is how to diffuse frustration and to best help the child and the parents identify constructive strategies around food and eating.

The literature on children’s eating behavior and weight outcome focuses on children’s self-regulation of energy intake and the relation of children’s eating behavior to their weight outcome. Clara Davis performed the pioneering work in this area and, in well-controlled environments with simply prepared foods, demonstrated that young children eat to energy needs by consuming what they like and deferring on less-preferred foods.^{1,2} Additional early work investigating infant response to changes in energy density of formula revealed that infants adjusted the volume of intake to reflect the energy density of the formula, decreasing volume of intake when energy density was increased.³ These results were considered to be evidence of an innate mechanism for self-regulation of energy intake.

Birch et al, in research with single meal protocols in the laboratory, have further investigated the ability of young children to self-regulate energy intake. Their studies have consistently revealed evidence of at least some degree of short-term regulation of energy intake.⁴ However, later work investigating individual differences in self-regulation of energy intake has suggested that the extent to which children show short-term compensation for changes in the energy content of the diet varies considerably and is related to children’s weight status such that children with higher adiposity demonstrate less evidence of short-term energy regulation.⁵ Similar patterns have been noted in school-aged children.⁶

A number of potential influences on children’s ability to self-regulate energy intake have been suggested and, when considered in the bioecological model, these include macro-level influences (ie, community level influences and

the greater food environment) through microlevel influences such as the family environment, parent-child interactions, and characteristics unique to the child (eg, temperament).⁷ Birch et al, through earlier research and from data collected on the Girls’ Needs cohort reported by Anzman and Birch in this issue of *The Journal*, have contributed substantively to this body of work.⁸

Parental feeding practices, particularly parental restriction of children’s access to highly palatable foods, have been reported to have robust relationships with children’s eating behaviors and weight outcome.⁹ Parents who report taking greater control of children’s intake have children who display less evidence of self-regulation of food intake, greater eating in the absence of hunger,¹⁰ and consumption of highly palatable foods after reporting they are no longer hungry.¹¹ Thus, whether parents’ feeding practices cause disinhibited eating on the part of children or whether parents are responding to inborn characteristics of the child is unclear.

The focus of the work by Anzman and Birch,⁸ child temperament as related to impulsivity and inhibitory control, has particular significance for beginning to tease out the sequence or directionality of the association between children’s eating and parental feeding styles. Inhibitory control, as defined by Rothbart et al, denotes an active process of inhibition: an “effortful control” or self-regulation.¹² Inhibitory control emerges late in infancy, continues to develop during the toddler and preschool years, and is reported to have good longitudinal stability.¹³ As such, this aspect of child temperament is considered to be at least partly biological and developmental in nature. Parent-child interactions, such as the degree of parental control, have been posited to contribute to the growth of children’s inhibitory control and its converse, impulsivity.¹⁴ Longitudinal study of the development of children’s self-regulation suggested that the extent to which parents were responsive and provided cognitive stimulation related to their children’s ability to delay gratification. These studies of children’s development of inhibitory control form the basis for the study by Anzman and Birch.

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