(用)

- 6. Morris JA, Blount RE, Savage RE. Recovery of cytopathic agent from chimpanzees with coryza. Proc Soc Exp Biol Med 1956;92:544-50.
- 7. Olicker A, Li H, Tatsuoka C, Ross K, Trembath A, Hibba AM. Have changing palivizumab administration policies led to more respiratory morbidity in infants born at 32-35 weeks? J Pediatr 2016:171:31-7.
- 8. American Academy of Pediatrics. Modified recommendations for use of palivizumab for prevention of RSV infections. Pediatrics 2009;124:1694-701.
- 9. Simoes EAF, Groothuis JR, Carbonell-Estrany X, Rieger CHL, Mitchell I, Fredrick LM, et al. Palivizumab prophylaxis, RSV and subsequent recurrent wheezing. J Pediatr 2007;151:34-42.
- 10. Yoshihara S, Kusuda S, Mochizuki H, Okada K, Nishima S, Simoes EAF. Effect of palivizumab prophylaxis on subsequent recurrent wheezing in preterm infants. Pediatrics 2013;132:811-8.
- 11. Blanken MO, Robers MM, Molenaar JM, Winkler-Seinstra PL, Meijer A, Kimpen JLL, et al. RSV and recurrent wheeze in healthy preterm infants. N Engl J Med 2013;368:1794-9.
- 12. Caliskan M, Bochkov YA, Kreiner-Moller E, Bonnelykke K, Stein MM, Du G, et al. Rhinovirus wheezing illness and genetic risk of childhoodonset asthma. N Engl J Med 2013;368:1398-407.
- 13. Edwards MR, Bartlett NW, Hussell T, Openshaw P, Johnston SL. The microbiology of asthma. Nat Rev Microbiol 2012;10:459-71.
- 14. Tomsen SF, van der Sluis S, Stensballe LG, Posthuma D, Skytthe A, Kyvik KO, et al. Exploring the association between severe RSV infection

and asthma: a registry-based twin study. Am J Respir Crit Care Med 2009:179:1091-7.

- 15. Zomer-Kooijker K, Uiterwaal CS, van der Gugten AC, Wilbrink B, Bont LJ, van der Ent CK. Decreased lung function precedes severe RSV infection and post-RSV wheeze in term infants. Eur Respir J 2014;44:666-74.
- 16. Miyairi I, DeVincenzo JP. Human genetic factors and RSV disease severity. Clin Microbiol Rev 2008;21:686-703.
- 17. Janssen R, Bont L, Siezen CL, Hodemaekers HM, Ermers MJ, Doornbos G, et al. Genetic susceptibility to RSV bronchiolitis is predominantly associated with innate immune genes. J Infect Dis 2007;196:826-34.
- 18. Martinez FD, Morgan WJ, Wright AL, Holberg C, Taussig LM. Initial airway function is a risk factor for recurrent wheezing respiratory illnesses during the first 3 years of life. Am Rev Respir Dis 1991;143:312-6.
- 19. Drysdale SB, Wilson T, Alcazar M, Broughton S, Zuckerman M, Smith M, et al. Lung function prior to viral lower respiratory tract infections in prematurely born infants. Thorax 2011;66: 468-73.
- 20. O'Brien KL, Chandran A, Weatherholtz R, Jafri HS, Griffin MP, Bellamy T, et al. Efficacy of motavizumab for the prevention of RSV disease in healthy Native American infants: a Phase 3 randomized double-blind placebo-controlled trial. Lancet Infect Dis 2015;15:1398-408.

Ventilation Remains the Key to Neonatal Resuscitation

reparedness is vital to successful neonatal resuscitation. Because it is not possible to predict perfectly which babies will need resuscitation, a person who can assess the newly born infant and initiate resuscitation should be present at all births; additional personnel with

the skills to perform a complete resuscitation, including endotracheal intubation,

should be immediately available.¹ Preparedness relies on prebriefing, whether a simple exchange of facts or a more formal group process occurring before a birth, to convey information from those who are responsible for the fetus and pregnant woman to those who will be responsible for the newborn. Prebriefing includes assessment of risk factors such as preexisting medical conditions, pregnancy complications, and difficulties arising during labor. Risk factors signal the pathophysiologic processes that may come into play and the interventions that may be needed. They help determine the people who need to be present at a birth and the roles they will play in delivering interventions and responding to potential complications. Prebriefing can be considered a process measure for resuscitation preparedness and high-quality perinatal care.

The report by Almudeer et al addresses a question that is central to preparedness for resuscitation: what risk factors are associated with endotracheal intubation?² Previous guidance on risk factors for resuscitation has been quite global; the 6th edition of the Neonatal Resuscitation Program Textbook lists over 40 antepartum and intrapartum factors associated with the need for neonatal resuscitation.¹ Using a provincial database of births in

See related article, p 55

Nova Scotia, the authors of the current study analyze the risk factors associated with intubation in a population of infants \geq 35 weeks gestation born between 1994 and 2014. Sixteen factors emerged with a statistically significant association with intubation,

including such conditions as hydrops, major fetal anomaly, prematurity, fetal distress, chorioamnionitis, general anesthesia, and hemorrhagic complications of labor and delivery. One prior prospective analysis examining the use of either positive-pressure ventilation or intubation reported similar associations.³ An acknowledged limitation of the current study is that absence of intubation does not necessarily mean that it was not needed and, conversely, performance of intubation does not mean that it was appropriate. The risk factors of diminished fetal activity, no prenatal care, and maternal adrenergic agonist medications were not investigated because the database lacked clear coding of those variables. Despite these limitations, the new analysis does strengthen the evidence base for risk assessment relative to resuscitation, which previously had relied heavily on consensus.4

S.N. serves as an evidence evaluator for neonatal ILCOR (International Liaison Committee on Resuscitation) and as editor of Helping Babies Breathe for the American Academy of Pediatrics.

0022-3476/\$ - see front matter. Copyright © 2016 Elsevier Inc. All rights reserved http://dx.doi.org/10.1016/j.jpeds.2015.12.080

How does the refined information on risk factors associated with intubation affect preparedness? When prebriefing for a delivery, the decision whether to have a person skilled in intubation in attendance or immediately available becomes clearer. Especially in settings where attendance at delivery takes skilled intubation providers away from other equally critical responsibilities, the reduction of calls to attend deliveries not resulting in intubation can improve overall efficiency and quality of care. At the level of the delivery unit or the health system, allocation of workforce resources can be made more objectively, providing that the risk profile of the patient population is available through a similar database. However, preparedness still requires that the person in attendance is capable of initiating resuscitation and mandates conscious planning around how intubation will be accomplished if needed. At every delivery, there needs to be 1 person capable of initiating effective ventilation and another person who can summon additional immediate help. Making intubation "immediately available," even for low-risk births in first-level facilities, may mean alerting an anesthesiologist or the emergency department physician of an impending delivery or it may mean calling a provider in from home to be on standby in case intubation is needed. Intubation can be a lifesaving intervention; the refinement of risk factors predicting intubation does not change the requirement for availability-only the proximity of the skilled person at the moment of birth.

It is especially pertinent to consider intubation in the context of the 2015 revised recommendations for management of infants born with meconium in the amniotic fluid. Almudeer et al caution that the significance of the association of meconium-stained amniotic fluid with endotracheal intubation must be interpreted in light of changing management over time. New guidelines no longer recommend routine intubation of depressed infants with meconium-stained amniotic fluid for tracheal suctioning, but rather suggest management with the usual initial steps of resuscitation and positive-pressure ventilation with bag and mask.^{5,6} However, there is continued need for a person who is immediately available and capable of intubation for a blocked airway or inadequate response to positive-pressure ventilation. Moreover, the provider responsible for positive-pressure ventilation needs to have mastery of that skill-achieving a mask seal to deliver adequate tidal volume, taking corrective steps to improve ventilation, and avoiding excessive inflation or asynchronous ventilation that may increase the risk of air leak. Although a larvngeal mask airway may provide an alternative to face mask ventilation when intubation is not feasible, it does not permit ready passage of a suction catheter to relieve airway obstruction with meconium. Although a person skilled in intubation may no longer be in attendance at every delivery complicated by meconium in the amniotic fluid, that person must still be immediately available.

There is an acute need to focus on mastery of airway management and effective ventilation during training as

performance of endotracheal intubation decreases with revised meconium management, increasing use of continuous positive airway pressure in the delivery room, and minimally invasive surfactant administration. As discussed in the accompanying article, several surveys have shown that pediatric trainees frequently do not master the skill of intubation during residency without deliberate focus on this skill. Other recent studies have highlighted how significant mask leak may compromise the effectiveness of bag-and-mask ventilation.⁷ The 2015 International Consensus on Science with Treatment Recommendations as well as the Neonatal Resuscitation Guidelines Update from the American Heart Association highlight the key role of ventilation in neonatal resuscitation and suggest that maintenance of skills likely requires more frequent refresher training than currently prescribed. Low-dose, high-frequency customized training with feedback on mask leak, tidal volume, and ventilation rate can improve technique.⁸ Team training with a focus on behavioral skills such as communication, leadership, and situational awareness becomes vital to respond successfully to an unexpected, complex resuscitation. Ventilation remains the key to neonatal resuscitation, with or without endotracheal intubation.

> Susan Niermeyer, MD, MPH Section of Neonatology University of Colorado School of Medicine Aurora, Colorado

Reprint requests: Susan Niermeyer, MD, MPH, Section of Neonatology, University of Colorado School of Medicine, 13121 E. 17th Ave, Mail Stop 8402, Aurora, CO 80045. E-mail: susan.niermeyer@ucdenver.edu

References

- Kattwinkel J, editor. *Textbook of Neonatal Resuscitation, 6th edition*. Elk Grove Village, IL: American Academy of Pediatrics and American Heart Association; 2011.
- Almudeer A, McMillan D, O'Connell C, El-Naggar W. Do we need an intubation-skilled person at all high-risk deliveries? J Pediatr 2016; 171:55–9.
- Aziz K, Chadwick M, Baker M, Andrews W. Ante- and intra-partum factors that predict increased need for neonatal resuscitation. *Resuscitation* 2008;79:444–52.
- **4.** Perlman J, Kattwinkel J, Wyllie J, Guinsburg R, Velaphi S, Singhal N, for the Neonatal ILCOR Task Force Group. Neonatal resuscitation: in pursuit of evidence gaps in knowledge. *Resuscitation* 2012;83: 545–50.
- Perlman JM, Wyllie J, Kattwinkel J, Wyckoff MH, Aziz K, Guinsburg R, et al. Part 7: neonatal resuscitation: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. *Circulation* 2015;132(16 Suppl 1):S204–41.
- 6. Wyckoff MH, Aziz K, Escobedo MB, Kapadia VS, Kattwinkel J, Perlman JM, et al. Part 13: neonatal resuscitation: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 2015;132(18 Suppl 2):S543–60.

Volume 171

- Kaufman J, Schmolzer GM, Kamlin CO, Davis PG. Mask ventilation of preterm infants in the delivery room. *Arch Dis Child Fetal Neonatal Ed* 2013;98:F405–10.
- van Vonderen JJ, Witlox RS, Kraaij S, te Pas AB. Two-minute training for improving neonatal bag and mask ventilation. *PLoS One* 2014;9:e109049.

Is the Risk of Diabetic Ketoacidosis Modifiable?



iabetic ketoacidosis (DKA), a most serious, lifethreatening acute complication of type 1 diabetes (T1D) in children, occurs in approximately 25%-30% of patients with newly diagnosed diabetes.^{1,2} Following the initial diagnosis, a small, yet important,

subgroup of patients will have 1 or more recurrent admissions for DKA.

The incidence of recurrent DKA in the US has been estimated at 8 per 100 person-years,³ but may be twice as high.⁴ In a major pediatric diabetes center, 80% of recurrent DKA occurred in 20% of the patients, and 60% of DKA occurred in 5% of the patients.³ Given the morbidity, low but definite mortality⁵ of complications of DKA (mainly cerebral edema), possible adverse effects of DKA on brain morphology and function,⁶ and the social burden and the economic cost of these admissions (estimated at \$90 million/year in the US⁷), several investigators have tried to identify risk factors for recurrent DKA in order to develop effective prevention strategies. Recurrent DKA is almost always related to omission or insufficiency of insulin delivery,² usually in association with inadequate diabetes self-care. It is probable that this condition is completely preventable, as suggested by the fact that the majority of compliant patients never experience DKA again after the initial diagnosis of T1D, and by the much lower incidence in countries with better access to medical care, such as Scandinavian countries.^{8,9}

In this issue of *The Journal*, Malik et al retrospectively examined the readmission rates for recurrent DKA in 12 449 children between age 2 and 18 years, followed at 42 US Children's Hospitals between 2004 and 2012.¹⁰ They examined multiple rolling 365-day intervals during a 5-year follow-up timeframe for each patient. In simple terms, when a patient was admitted for DKA, the patient was tracked for evidence of readmission to the same hospital in the following 365 days. The main outcome for their study was the maximum number of DKA admissions within any 365-day interval during a 5-year follow-up period for each patient. The objectives of the study were: (1) to determine risk factors predicting DKA readmission; and (2) to identify differences in these factors within hospitals and across hospitals. The results of the study were notable because a high percentage (28%) of patients admitted for DKA (first and repeat episodes not

DKA	Diabetic ketoacidosis
T1D	Type 1 diabetes

determined) were readmitted within the next 365 days. There was a "hierarchy" of factors associated with the relative risk of readmission (expressed as OR) across all hospitals. Non-Hispanic Black race, public insurance (used as a proxy for low socioeconomic status), and age

See related article, p 104

ticle, p 104 ≥ 12 years were the most important (OR 2.40-1.97); female sex and mental health comorbidity also contributed significantly (OR approximately 1.40). The hierarchy of risk factors was different at individual hospitals, and patients at some hospitals did substantially better than others, in as much as they had a low risk of readmission. This suggests that "local" factors may significantly affect the outcome of patients with T1D.

How relevant is the study by Malik et al to clinical practice? The risk factors they describe for recurrent DKA are not new, and had already been characterized in previous studies.^{3,7,11-13} What is new is the fact that the study showed clear variability in how hospitals "perform" in terms of readmission rates. Unfortunately, the study could not determine whether the variability was related to patient/population factors, hospital factors, or a combination of the two. Specific characteristics of the populations gravitating around each hospital, pattern of diabetes education or treatment at each center, including diabetes educator/patient ratio and strength of the support provided by social services or psychologist may have played a role, but this is speculative. Other limitations of the study stem from its retrospective nature, and the fact that data were harvested from the Pediatric Health Information System, an information hub which provides anagraphical, rather than clinical, data on patients. Thus, no information could be extracted on other potentially important risk factors, such as diabetes duration, diabetes control, total insulin dose, adequacy of diabetes education at diagnosis, frequency of outpatient visits, all of which were addressed in previous studies,^{3,7,11-13} and some of which (elevated Hemoglobin A1c especially) are powerful predictors of readmission. Finally, the low readmission rate in some of the "better-performing" hospitals could be explained in part by a larger number of poorly compliant patients moving to, and/or being treated at, other hospitals in the area for further episodes of DKA.

The authors declare no conflicts of interest.

^{0022-3476/\$ -} see front matter. Copyright © 2016 Elsevier Inc. All rights reserved. http://dx.doi.org/10.1016/j.jpeds.2016.01.057