apoptotic pathway. Use of immunoprecipitation experiments at different developmental time points after receptor agonism may explain whether this is an alteration in receptor signaling or changes in receptor expression with age. What does appear to be known is that $p75^{NTR}$ expression and signaling is not only temporally but also spatially dependent on some unknown intracellular mechanism. Studies to characterize $p75^{NTR}$ expression and its coupling with known partners (*e.g.*, Trk) at varying ages are currently underway in our laboratory. The expectation is that these studies will provide more detail about the mechanisms by which isoflurane injures developing neurons.

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Difficult Mask Ventilation and Neuromuscular Blockade

To the Editor:—We read with interest the article by Kheterpal *et al.* [1] regarding impossible mask ventilation. This is a very important but rare event, and this large study gives us a clear idea about its incidence and, for the first time, what the associated risk factors are.

We note that in all but 4 of the 77 cases of impossible mask ventilation, the patients had received neuromuscular blockade "in the process of induction or management of the airway," with succinylcholine being used in 65 patients and a nondepolarizing agent in the remaining patients. However, it is not clear at what stage of airway management that the neuromuscular blocker was administered in these cases—was it before difficulty with mask ventilation being encountered or given after problems occurred to improve the situation, and did ventilation indeed improve? Furthermore, only 19 patients (25%) proved difficult to intubate, which suggests that there was opportunity for improving the conditions for mask ventilation. Kheterpal *et al.* do go on to discuss the problem in assessing the role of muscle relaxants in mask ventilation difficulties, but the documentation for each case did not include an assessment of mask ventilation before and after neuromuscular blockade. It would be interesting to note if there is a difference in the incidence of impossible mask ventilation with or without neuromuscular blockade being given at induction (before attempts at mask ventilation). This may be an area for further investigation, although as with this study, a large population sample would be required.

In our experience, optimum depth of anesthesia and neuromuscular blockade provide the best conditions for both mask ventilation and tracheal intubation (in patients in whom an awake technique, transtracheal catheter, or awake tracheostomy are not indicated). Neuromuscular blockade given at induction and before attempts at mask ventilation is the most common practice in our institution for patients requiring tracheal intubation. In addition, we have found that using intermittent positive pressure ventilation by means of a Penlon Nuffield 200 ventilator (Penlon Ltd., Abingdon, United Kingdom) while holding a mask is beneficial for assessment of adequacy of mask ventilation and also useful for training. This approach has the advantage of allowing a two-handed mask technique for more challenging airways and continual monitoring of airway pressure from the pressure gauge on the ventilator. Monitoring airway pressure in this way provides an objective measure of the seal that is achieved with the mask and patency of the airway. Mask technique can then be optimized by reference to clinical signs (*e.g.*, chest expansion), airway pressure/peak pressure, and capnography. We also encourage initial management of the airway without use of an oropharyngeal/Guedel airway to improve and optimize these fundamental airway skills. Mask ventilation is our core skill, and we believe subjective and objective assessment throughout training is required to maintain this art and limit airway disasters.

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In Reply:—We thank Drs. Myatt and Patel for their interest in our data and comments. We agree that detailed, controlled data collection regarding the ease or difficulty of mask ventilation before and after administration of neuromuscular blockade would be of great interest. Unfortunately, as our original manuscript mentioned,[1] collecting these data using a large observational dataset is difficult. Aggregation of a 50,000-patient dataset has necessary limitations. Although observational data are exceptional for establishing the real-world effectiveness

of different clinical management strategies, they are suboptimal for evaluating the optimal efficacy of a specific strategy under ideal circumstances.[2]

It is not feasible to use a large observational dataset to define the impact of neuromuscular blockade on mask ventilation because of several issues: First, asking providers to document additional elements and attempt mask ventilation before neuromuscular blockade solely for research purposes may require institutional review board evaluation and patient consent. Second, the acuity of the induction period demands a parsimonious approach to documentation in general. Third, it would be difficult to control confounding clinical factors such as depth of anesthesia, dosage of neuromuscular blockade, experience of providers, mask ventilation technique, and timing of mask ventilation attempts.

Goodwin performed a prospective, controlled trial evaluating the impact of neuromuscular blockade in 30 patients with normal airways.[3] Contrary to our clinical experience and that espoused by Dr. Myatt, they found that neuromuscular blockade did not alter the efficacy of mask ventilation, measured by tidal volume. Because the studied population was limited to patients with normal airways, everyday clinicians are left to make decisions without data. Patients exhibiting risk factors for difficult mask ventilation such as obesity, limited jaw protrusion, bearded facial hair, advanced age, oropharyngeal disproportion, and a history of snoring[4] may be a population worthy of a controlled, prospective study. Such a study would prove to be time-consuming, expensive, difficult, and impractical, given the low incidence. Until then, our observational data describing the use of neuromuscular blockade in patients with impossible mask ventilation may have to suffice.

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Anesthesia-related Mortality

To the Editor:—We have read with great interest both the editorial of Dr. Lagasse[1] and the article of Li *et al.*,[2] which were related to the epidemiology of anesthesia-related mortality in the United States. The study by Li *et al.*[2] used the data from the National Vital Statistics System and the International Classification of Diseases codes (10th revision) to assess mortality related to anesthesia in the United States between 1999 and 2005. A similar study has been performed in France in 1999 and was correctly referenced by the authors.[3] The major advantage of such a methodology is the completeness of mortality data retrieved from the National Vital Statistics System. However, when trying to identify deaths related to anesthesia, and to describe the precise degree of imputation, some problems arise.

First, the coding system is not detailed enough to capture the precise mechanism(s) that led to death and to ascertain a causal relationship. To assess more precisely the pathophysiological mechanism(s) that led to death, and subsequently to clarify the relation to anesthesia in the sequence of events, an expert analysis remains necessary, which may even be better replaced by a peer discussion with the anesthesiologist in charge of the case and who reported the death.

Second, as Dr. Lagasse noticed in his Editorial, the 10th revision of International Classification of Diseases is curiously quite poor regarding anesthesia. Items are more numerous for anesthesia for pregnancy and labor than for anesthesia in general. They explore mainly the surgical time and are mostly limited to anesthetic medication side effects or overdose. What about aspiration occurring during an emergency procedure, for example? Also, what about hemorrhage and/or delayed blood transfusion? This could be one of the limitations of this method, as the authors have noticed themselves in the discussion section of the article. Maybe the use of specific keywords related to anesthesia practice, in addition of the selection of International Classification of Diseases codes as described, could enhance the sensibility of the filter. However, even adding these suggestions might not be powerful enough to capture all cases. In the experience of the Mortality Research Group of the French Society of Anesthesia and Intensive Care,[3] we have experienced that in some cases death certificates did not mention any specific International Classification of Diseases code or any previously determined specific keyword. The patients' files could be included in the survey only because researchers had chosen to select also death certificates in which a surgical (or invasive) procedure was mentioned.

Third, although one could manipulate in many ways the method to select death certificates to detect all cases that have a relation to anesthesia, is it the real problem? The specificity of the filter will never reach 100 percent. We only assess the visible part of the iceberg. Maybe it would be more efficient to monitor the same indicator along time as the trend is likely a valuable marker, even if absolute data are very approximate. It could thus be very interesting to choose an indicator both strongly related to anesthesia and reproducible to assess over time the trend of anesthesia-related mortality through a national mortality database, rather than simply obtain punctual data through a great nationwide survey.

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The above letter was sent to the author of the referenced editorial. The author declined to reply.—James C. Eisenach, M.D., Editor-in-Chief.