severe lung disease and its associated episodes of hypoxemia and prolonged ventilation, neurologic malformations, and cerebral palsy. I would suggest that the complex medical history of my own son is representative of the learning disabled who have had multiple anesthetic exposures. His American Society of Anesthesiologists physical status never exceeded II during his four anesthetics as a young child, despite the fact that during that critical period of development, he experienced neonatal sepsis, disseminated osteomyelitis, hepatic insufficiency with attendant coagulopathy, postfebrile partial complex seizure disorder, perioperative hemorrhage, and postoperative anemia. I have searched for explanations for his learning disabilities, but not once in 17 yr have I thought to attribute them to his anesthetic exposures.

A rational understanding of the potential neurotoxicity of anesthetic and sedative agents in the developing brain requires an animal model that closely mimics the clinical reality of serious illness and surgical stress requiring intervention. Clinical reviews, both retrospective and prospective, that address the association of anesthetic exposure and compromised neurodevelopment in young children are critical to our understanding. A threshold toxic dose should be sought and the possibility of a biphasic response of the developing brain should be considered, much like oxygen exposure where both hypoxia and hyperoxia result in permanent deficits. Paracelsus stated that "Poison is in everything, and no thing is without poison. The dosage makes it either a poison or a remedy." His observation is as relevant today as it was nearly 500 yr ago.

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Surgical Diagnosis Is an Important Variable to Consider in Postanesthesia Exposure–associated Learning Disabilities

To the Editor:—We commend Dr. Wilder *et al.*[1] for their work titled "Early Exposure to Anesthesia and Learning Disabilities in a Population-based Birth Cohort." In their article, they report that patients younger than 4 yr, with two or more exposures to general anesthesia, had a greater proportion of learning disabilities (LDs) compared with children who had one or no exposure to general anesthesia. This represents a clinically important epidemiologic correlate to compliment the worrying animal observations demonstrating the detrimental effects of general anesthesia on the developing brain.

A primary assumption in cohort analyses is that the groups observed are the same before exposure. However, children requiring anesthesia for surgical treatment may be inherently different from those who do not; these differences may present unique factors that predispose to LDs independent of anesthesia *per se*. In particular, we are concerned that a subpopulation at risk for learning disabilities—children undergoing ears, nose, and throat surgery—is overrepresented. Typical ears, nose, and throat surgeries in this age group include adenotonsillectomy and bilateral myringotomy with tympanostomy tube placement. The former is associated with obstructive sleep apnea, which can result in neurocognitive defects[2]; the latter may be associated with otitis media with effusions, which can yield poor performance in expressive speech and math testing in younger children.[3]

These coexisting conditions may have skewed the diagnosis of LD in this population. This is relevant because children tested within a short period of time from their ears, nose, and throat surgery may not have had sufficient time to "catch up" with their peers in terms of testing, should the surgery have improved their condition. Furthermore, given the frequency of achievement tests administered to the cohort population, is it possible to find children who no longer met LD definitions at some time point during follow-up testing? This would be of particular interest for those children undergoing ears, nose, and throat surgeries.

In addition, we are concerned that the third definition of LD included patients in the low-average IQ range *versus* average intelligence. Moreover, using a cutoff of 1.75 SDs below their predicted standard score, as opposed to the conventional 2 SDs, might be an oversensitive method of identifying patients with LDs.

We are interested to know whether the authors could remove patients who underwent adenotonsillectomy and bilateral myringotomy with tympanostomy tube surgeries from the analysis and apply conventional definitions of LD to determine whether a relation between general anesthesia and LD persists.

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