

Hernia Repair, Anesthetic Exposure, and Academic Performance in Children

To the Editor:

We read with interest the recent article by Hansen *et al.* in which the authors analyzed academic performance in adolescents after inguinal hernia repair in infancy.¹ The authors have made an important contribution to the small but growing body of human studies pertaining to the critically important issue of anesthesia-related neurotoxicity in young children. Although not mentioned by the authors in their discussion, the absence of a finding suggestive of learning difficulties among those exposed to inguinal hernia repair as infants is consistent with that of our study of learning disabilities after anesthetic exposure in young children in Rochester, Minnesota.² The study by Hansen *et al.* and our own study failed to demonstrate an effect of a single exposure on outcomes among all subjects in both birth cohorts (our study used learning disability, rather than academic performance, as the outcome). However, we found that exposure to two or more anesthetics before age 4 yr significantly increased the risk for a learning disability developing before age 18 yr.

Hansen *et al.* did not (or could not) differentiate those having multiple exposures because the need for anesthesia appears not to be included in the Danish registry (the need is inferred based on the procedure). It is also not clear how Hansen *et al.* dealt with children who underwent procedures other than inguinal hernia repair. If procedures other than hernia repair were not excluded from both groups, it would appear that, rather than examining the effect of anesthesia *per se*, the study examines the effect of *hernia repair* because both the hernia repair cohort and no hernia repair cohort potentially would include children exposed to anesthesia for other procedures, including some children with multiple exposures. It is not possible from the manuscript to determine what inclusion or exclusion criteria were used, making it difficult to properly interpret these important data. Likewise, it is unclear whether both inpatients and outpatients were included in the analysis. It appears from the reference cited by the authors (ref. no. 28) that outpatients were not included because as according to that particular reference, outpatients were included in the Danish National Hospital Register only after 1995. If true, this may have excluded many cases and made them available as potential controls (a potential misclassification bias).³

Investigators in this area all struggle to ensure that the best possible data are available to assist providers, parents, and public health officials in determining the safety of the anesthetic and other drugs that we and our colleagues use each day. The results of all existing and planned human studies in

this area, each of which has its own limitations (especially with potential unmeasured confounders) and outcome definitions, need to be considered carefully. Clarification of these issues should not detract from the important work undertaken by the authors in the performance of this large study.

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References

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In Reply:

We appreciate and share Flick and Warner's concern that multiple surgical procedures early in life can be associated with learning disabilities later in life, as suggested in their cohort study of 593 children younger than 4 yr.¹ Of those, 100 (16.9%) children underwent two episodes of anesthesia and 44 (7.4%) underwent three or more such episodes and experienced significant comorbidities known to be associated with learning disabilities. Thus, the extent to which anesthesia may or may not contribute to these remains to be elucidated.^{2,3}

Our research is based on more than 45,000 Danish children who underwent surgery before the age of 1 yr during the period 1977-1990.

In our first study, we found no evidence for a general effect of anesthesia on academic performance.⁴ For several reasons, we chose to focus on children born between 1986 and 1990 who underwent surgery in the first year of life for inguinal hernia (n = 2,689) compared with a 5% random sample of the whole population (n = 14,575). Those reasons are: (1) Such a study will have more public health relevance because a much larger proportion of infants undergo only one episode of general anesthesia (surgery) in infancy, (2) children undergoing multiple episodes of anesthesia (surgeries) are likely to have more severe underlying conditions that may be the reason for later learning disabilities, and (3) our approach is likely to be unbiased or overestimate the effect of