

Postoperative Apnea in Former Preterm Infants

General Anesthesia or Spinal Anesthesia—Do We Have an Answer?

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A LOT has changed in neonatology and pediatric anesthesiology since the 1980s when the studies that formed the current recommendations for anesthesia and perioperative care for young infants at risk of postoperative apnea were conducted. The story behind these studies is worth retelling to understand the contribution of the study by Davidson *et al.*¹ in the current issue of *ANESTHESIOLOGY*. Noteworthy, the study by Davidson *et al.*¹ is the largest one conducted on postoperative apnea and the first in over 20 yr!

Davidson *et al.*¹ reported on the incidence of postoperative apnea as a secondary outcome in a multicenter randomized prospective trial (General Anesthesia compared to Spinal Anesthesia study) of 722 young infants comparing general anesthesia (GA) with regional anesthesia (RA). Although the General Anesthesia compared to Spinal Anesthesia study's primary outcome was neurodevelopment to investigate anesthetic neurotoxicity, the study represented an opportunity to examine postoperative apnea after GA *versus* RA. The key findings were less early apnea (initial 30 min in postanesthesia care unit [PACU]) after RA, similar late apnea (after PACU) after RA and GA, and occasional life-threatening apnea in PACU or the ward after either RA or GA. Despite the passage of time and a lot of changes in health care, the results of the study support the original studies,^{2–5} especially reaffirming the longstanding recommendation to monitor this population postoperatively for life-threatening apnea.^{2–6}

The story of postoperative apnea began more than 30 yr ago with an index case: death of a healthy



“The main difference between [general and regional anesthesia] was the timing of the apnea, being more common in the PACU after [general anesthesia].”

former premature infant after an uneventful general anesthetic and PACU for an inguinal hernia repair in which apnea and cardiac arrest occurred during transport to the ward. From 1982 to 1992, many studies^{2–5,7–9} investigated postoperative apnea in infants undergoing surgery during the initial months of life. These studies concluded that the incidence of postoperative apnea is inversely proportional to post-conceptual age (PCA); younger gestational age and anemia are additional risk factors; postoperative apnea can occur even though there is no preoperative history of apnea; the first apnea usually occurs in PACU, but it can also occur several hours later on the ward; and apnea is usually associated with airway obstruction making detection by bedside monitors and observation less reliable.

There are various recommendations for outpatient surgery, from 44 to 60 weeks PCA in prematurely born infants.^{2–6,9} This variability stems from uncertainty in the data related to small sample sizes and variable incidences of postoperative apnea among studies and existence of medico legal cases for death from postoperative apnea. In 1995, Coté *et al.*⁵ combined the previous studies yielding 384 infants in an attempt to better establish outpatient surgery guidelines. The study by Coté *et al.*⁵ revealed that postoperative apnea was twofold greater when continuous recording devices were utilized compared with bedside monitors and observation, and that bag mask ventilation for apnea occurred in PACU and not on the ward. Statistical models reaffirmed the inverse relationship of postoperative apnea with PCA and gestational age and increased risk with anemia (hematocrit

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< 30%), although a safe age for outpatient surgery could not be determined because of insufficient sample size.⁵ For example, Fisher¹⁰ calculated that 300 patients for each week PCA would be required to ensure with 95% probability that the incidence of apnea would not exceed 1% in a particular age group. Accordingly, the recommendations for outpatient surgery have remained uncertain and reflect the risk tolerance of the anesthesiologist.

This brings us to the current study by Davidson *et al.*¹ A lot has changed in neonatal and perioperative care since 1995 to suggest that the epidemiology of postoperative apnea and need for postoperative monitoring might be different today. In particular, the shorter acting anesthetic sevoflurane has replaced halothane, and surfactant administration has decreased lung morbidity in premature infants.

Davidson *et al.*¹ compared the rates of postoperative apnea between GA *versus* RA for inguinal herniorrhaphy in infants younger than 60 weeks postmenstrual age born older than 26 weeks gestation without risk of adverse neurodevelopmental outcome. The data were analyzed as intent-to-treat (ITT) or as per protocol. For the ITT, there were 358 in GA and 361 in RA of whom 70 were converted to GA, which decreased RA numbers for the as per protocol. The overall incidence of postoperative apnea was 6.1% in prematurely born and 0.3% in full-term infants and was not different between RA and GA. However, the incidence and severity of early apnea (0 to 30 min in PACU) were less in RA. Of those with postoperative apnea, 86% in GA and 50% in RA received interventions including manual stimulation, bag mask ventilation, and cardiopulmonary resuscitation. Of those receiving bag mask ventilation, one infant was 53 weeks postmenstrual age (34 weeks gestation and 55 weeks PCA), one infant was full term (37 weeks gestation and 45 weeks PCA), and two infants manifested the first apnea 6 to 7 h postoperatively (29 weeks gestation and 43 weeks PCA; 30 weeks gestation and 42 weeks PCA) both in RA group. In statistical models, the risk of apnea was associated with prematurity and decreasing gestation and postmenstrual age. Anesthetic and intraoperative factors were not associated with postoperative apnea. Although apnea in PACU was predictive of apnea on the ward, the absence of apnea in PACU did not exclude apnea from occurring on the ward. These findings agree with the historical studies.^{2–5}

An issue that greatly clouds the Davidson *et al.*¹ study is the lack of standardized postoperative monitoring with the result of a high likelihood for missed events and late detection of apnea with increased need for life-saving interventions (*e.g.*, bag mask ventilation). Apnea was determined by research assistant observation in PACU and retrospective chart review after that. Of the infants, only 88% were monitored with pulse oximetry, 33% with electrocardiography, and 35% with a respiratory rate monitor. Standardized, high-reliable postoperative

monitoring might have prevented the nearly 2% incidence of life-threatening events from occurring in the study by Davidson *et al.*¹

Two additional observations warrant comment. First, there is an appreciable failure rate with RA: 19% of infants in the ITT RA arm were converted to GA or RA with sedation because of inadequate RA or preference by anesthesiologist or surgeon for GA. Interestingly, apnea after RA with sedation was similar to that of RA alone. Previous studies^{11,12} were conflicting on the effect of sedation with RA. Thus, the weight of evidence suggests that RA with sedation is no different than RA alone and better than GA. Second, Davidson *et al.*¹ did not find an association of postoperative apnea with anemia, at odds with previous studies.^{5,7} This may be a result of the analysis with insufficient numbers, in that risk of apnea was assessed by “increase per unit” as opposed to by group (normal *vs.* anemia).

In conclusion, despite medical advances during the past few decades, inguinal hernia repairs in former premature infants using RA, RA with sedation, or GA are still associated with life-threatening apnea, which usually begins in the PACU but can also begin several hours later on the ward. The main difference between GA and RA was the timing of the apnea, being more common in the PACU after GA. Thus, the study by Davidson *et al.*¹ demonstrates a slight advantage of RA. Anesthesiologists should continue their current guidelines for postoperative monitoring and outpatient surgery in former premature, even though a lot has changed during the past 30 yr!

Competing Interests

The authors are not supported by, nor maintain any financial interest in, any commercial activity that may be associated with the topic of this article.

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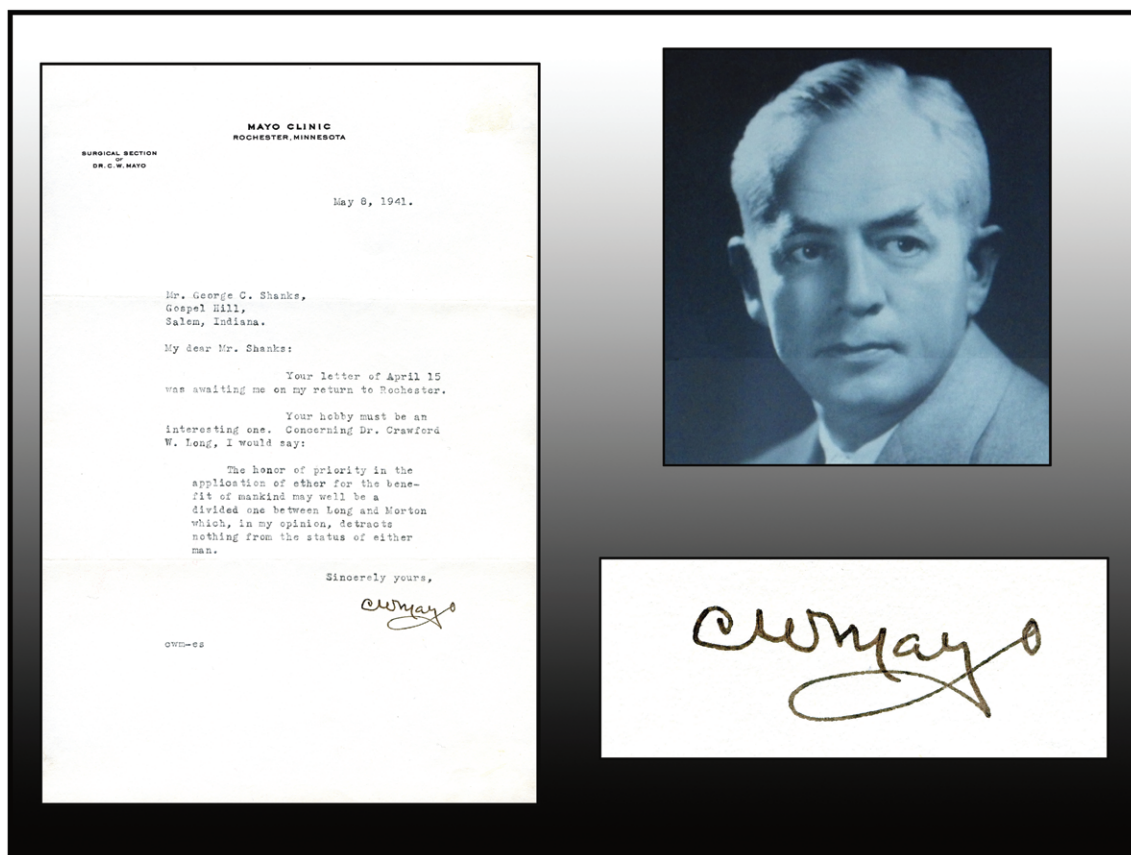
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“Between Long and Morton”? C. W. Mayo Opines



On April 15, 1941, from Salem, Indiana, a Mr. George C. Shanks wrote a letter to Dr. Charles W. “Chuck” Mayo (*upper right*), son of Mayo Clinic cofounder Charles H. “Charlie” Mayo, M.D. Mr. Shanks was requesting Dr. C. W. Mayo’s view on whether Crawford Long or William Morton deserved the credit for pioneering surgical etherization. On May 8, Dr. Mayo signed a typewritten response (*left*) opining that, “The honor of priority in the application of ether for the benefit of mankind may well be a divided one between Long and Morton which, in my opinion, detracts nothing from the status of either man.” (Copyright © the American Society of Anesthesiologists, Inc.)

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