

Postoperative Apnea in a Full-Term Infant with a Demonstrable  
Respiratory Pattern Abnormality

CHARLES J. COTÉ, M.D.,\* DOROTHY H. KELLY, M.D.†

A number of studies have reported a high incidence of postoperative apnea in ex-premature infants returning for elective surgical procedures.<sup>1-5</sup> These papers emphasize the importance of a careful preoperative history and some have attempted to define that period of time post-conception during which the patient is most likely to be "at risk" for developing postoperative apnea. We report a full-term apparently healthy infant who unexpectedly developed apnea and bradycardia in the recovery room following an uneventful general anesthetic.

## CASE REPORT

H.S. was the 3.6-kg product of a 31-yr-old G4P3Ab1 who underwent an uneventful delivery at 39 weeks gestational age, and was discharged at 2 days. The patient was breast fed, had gained 0.5 kg since birth, and neither the mother nor patient were receiving medications. At 16 days of age she was scheduled for outpatient cystoscopy and surgical drainage of an imperforate hymen (41.5 weeks postconceptual age). She was the first case of the morning and anesthesia was induced and maintained with halothane, nitrous oxide, and oxygen. After induction, an iv catheter was inserted and 5% dextrose in lactated Ringer's solution was administered. Paralysis with 2.0 mg atracurium was achieved and a 3-mm ID endotracheal tube was inserted. The surgical procedure lasted 45 min at which time neostigmine 0.5 mg and atropine 0.2 mg were administered; when the train-of-four response indicated reversal of the effects of atracurium, the child was awakened by discontinuing halothane and having her breath 100% oxygen. At no time during the anesthetic was there any untoward event as documented by continuous measurement of expired carbon dioxide, pulse oximetry, electrocardiogram, temperature, and blood pressure. The infant received 150 ml of IV fluid. As the child was awakening, spontaneous respirations were allowed to return. While the trachea was still intubated, it was noted that the child had a periodic-type breathing pattern and had brief periods of apnea (less than 10 s). After several minutes, the breathing pattern became more regular, the child opened her eyes, moved all extremities well, and appeared alert and vigorous. At this

point the endotracheal tube was removed. The child was observed while breathing room air for several minutes and then transported to the recovery room. In recovery it was noted that the periodic breathing pattern returned; initially this was not accompanied by bradycardia. The patient's vital signs were stable with heart rate 140-150 beats per min, respirations 30-40 breaths per min, and rectal temperature 37°C. Forty five minutes postanesthesia, the infant was breast fed; during breast feeding it was noted that the child's heart rate increased to 200 beats per min, respirations increased to 70 breaths per min, and the oxygen saturation decreased to 85%. The frequency of the periodic breathing pattern and the return of apneic spells, as well as several episodes of bradycardia (heart rate in the 80s) with cyanosis all responding to stimulation, prompted an unscheduled hospital admission to the Intensive Care Unit for more careful observation. The child was observed for 3 days and did not have any further apneic spells associated with cyanosis or bradycardia. Three days after anesthesia (20 days of age), a full sleep study was performed in the pulmonary medicine laboratory with electroencephalographic monitoring, pneumogram, oxygen saturation, expired carbon dioxide, and electrocardiogram. The child was found to have multiple episodes (30-40 per h) of transient oxygen desaturation (saturation < 90% to a minimum of 75%), expired carbon dioxide values as high as 53 mmHg during both rapid eye movement (REM) sleep and quiet sleep, and multiple episodes of brief apnea (5-9 s during quiet sleep and 4-7 s during REM sleep); periodic breathing was 3.0%. Two episodes of obstructive apnea were also noted.

In view of this markedly abnormal respiratory pattern, the child was administered theophylline (7 mg/kg for 24 h) and repeat sleep studies demonstrated a normal respiratory pattern. The infant's respiratory pattern was monitored at home with an apnea monitor and the mother noted one episode of "duskyess" 3 weeks after discharge which responded to mother's stimulation. Repeat sleep studies were performed at 6-week intervals and the child continued to receive theophylline for 3 months at which time the theophylline was discontinued; a repeat sleep study was normal. Respiration was monitored at home with the apnea monitor for an additional month. At 18 months of age she is completely normal. The family history was negative for sudden infant death syndrome (SIDS) and apnea of infancy.

## DISCUSSION

Apnea following general anesthesia was first described in ex-premature infants by Gregory and Steward.<sup>1-2</sup> Liu *et al.* prospectively examined 173 full-term infants and 41 ex-premature infants (<37 weeks gestational age). She found no episodes of apnea in the full-term infants but a significant number of the ex-premature infants, particularly those with a prior history of apnea and those less than 41 weeks postconception developed postoperative apnea; all categories of surgical procedures were included.<sup>3</sup> Welborn studied 86 infants—of which 38 were ex-premature infants—undergoing inguinal herniorra-

\* Associate Professor of Anaesthesia, Harvard Medical School, Associate Anesthetist, Massachusetts General Hospital, Boston, Massachusetts.

† Associate Professor of Pediatrics, Harvard Medical School, Associate Pediatrician, Massachusetts General Hospital, Boston, Massachusetts.

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Address reprint requests to Dr. Côté: Department of Anesthesia, Massachusetts General Hospital, Boston, Massachusetts 02114.

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phy; none of the 86 infants developed apnea but 14 of 18 ex-premature infants, all less than 44 weeks postconception, developed periodic breathing.<sup>4</sup> Kurth found episodes of apnea following 25 of 49 surgical procedures in ex-premature infants.<sup>5</sup> Apneic events were inversely related to gestational age and apneic spells were noted in 14 of 18 patients who had abnormal pneumograms. Infants with apnea had a mean postconceptual age of 44 weeks. Interestingly, Kurth observed apnea in ex-premature infants without a prior history of apnea and four of these infants were older than 48 weeks postconception. The majority of apneic spells occurred in the recovery room and only one infant required mechanical ventilation. Apneic episodes were observed up to 12 h postanesthesia. The results of several other studies reported as abstracts have described similar findings, *i.e.*, postanesthesia apnea may occur in ex-premature infants with or without a prior history of apnea, tends to occur in younger infants (<47 weeks postconceptual age), and usually occurs in the recovery room but may also occur after the patient has left recovery.<sup>‡§¶</sup>

Although the anesthesia community has been amply warned about the association between postanesthetic apnea and ex-premature infants who are less than 60 weeks postconception age, there are few published data on the incidence of apnea in full-term infants. Liu *et al.* examined 173 full-term infants and did not observe apnea in the "normal" full-term infants; the postconceptual ages of these patients was not reported and continuous pneumographic recordings were not made.<sup>3</sup> Welborn *et al.* examined postoperative pneumograms in ex-premature and full-term infants; 48 full-term infants had normal postoperative pneumograms (only 7 were <44 weeks post conception).<sup>4</sup> The case presented is the first in a full-term infant documenting by sleep pneumogram an abnormality of respiration initially recognized while recovering from general anesthesia. Our patient did not meet all the criteria necessary to label her a "near miss" SIDS infant because she did not have a severe episode either in the hospital or at home that required resuscitation. However, she clearly had an abnormality of respiration consistent with the pattern observed in some infants susceptible to SIDS.<sup>6-9</sup> Additionally, her sleep respiratory pattern became normal following theophylline therapy.

Tetzlaff *et al.* observed a single episode of apnea fol-

lowing one anesthetic and found periodic breathing following a second anesthetic in a 42 weeks postconception infant (the same age as our patient).<sup>10</sup> Awake and asleep polysomnographic study with pneumogram and oxygen saturation monitoring failed to reveal an abnormality of respiration and the child was discharged home without the apparent need for continued apnea monitoring. The child demonstrated "postoperative instability of respiratory control." This patient was, however, a twin and also had bilateral congenital cataracts suggesting the possibility of other risk factors, *e.g.*, possible congenital viral infection, multiple births. Noseworthy *et al.* reported a full-term infant with extrophy of the bladder operated upon at 30 h of age.<sup>11</sup> Four hours after tracheal extubation the child developed apnea and bradycardia requiring resuscitation; no specific cause of the apnea was discovered. This child did not receive any opioids or regional nerve block; it is possible that abdominal pain contributed to the development of apnea. The child's respiratory pattern was carefully monitored in the Intensive Care Unit and an apnea monitor was used following discharge. Unfortunately, no sleep respiratory studies were reported and apparently no other apnea spells were documented by the apnea monitor. Neither of these patients had persistent, demonstrable pulmonary abnormalities which persisted beyond the immediate postoperative period.

The "normal," full-term infant will have approximately  $0.7 \pm 1.0\%$  of breathing time spent in a periodic breathing pattern.<sup>12</sup> Any full-term infant with greater than 3.5% periodic breathing should be considered to have an abnormal respiratory pattern.<sup>12,13</sup> This abnormal breathing pattern and the associated propensity toward apnea, may be exaggerated by such factors as anemia, hypothermia, hypoglycemia, hypoxemia, hypercarbia, mechanical obstruction to the airway, and drugs which may alter the normal response to oxygen and carbon dioxide.<sup>6-9,14</sup> Certainly the operating room environment and the anesthetic agents provide many of the conditions necessary to exacerbate the propensity toward apnea. Our patient was not hypothermic, hypoglycemic, anemic, or hypoxic. Controlled ventilation prevented hypercarbia as documented by expired carbon dioxide measurement. The only drugs that the patient received were nitrous oxide, halothane, and atracurium; certainly halothane has been demonstrated in adults to alter the normal response to hypoxemia and hypercarbia.<sup>14</sup> Therefore, it is not unreasonable to expect an exaggeration of this effect in a neonate. Partial residual neuromuscular blockade, although possible, was unlikely with a normal train-of-four response following reversal of the effects of atracurium and, clinically, the child appeared vigorous. It was evident that the clinical manifestations of the immature respiratory pattern markedly improved on the second and third postoperative days. This child, however, still had very striking abnormalities that were recorded days after one would

‡ Mestad PH, Glenski JA, Binda RE, Jr. When is outpatient surgery safe in preterm infants? (abstr). *Anesthesiology* 69:744, 1988.

§ Vanik PE, Warner LO, Teitelbaum DH, Martino D, Caniano DA, Servick J. Inguinal herniorrhaphy in young infants: Perioperative problems. Presented at the Section on Anesthesiology, American Academy of Pediatrics, May 1988.

¶ Malviya S, Swartz J, Lerman J. Are all preterm infants less than 60 weeks post-conceptual age at risk for postoperative apnea? (Suppl). *Anesth Analg* 68:S1-S321, 1989.

expect direct effects due to anesthetic agents; this is the first report of a demonstrably abnormal respiratory pattern in a full-term infant first noted following general anesthesia. This was not expected in a full-term healthy child who had gained weight and did not have a surgical procedure that would cause pain.

This child initially demonstrated a high frequency of periodic breathing in the operating room and the recovery room; this respiratory pattern is clearly abnormal in a full-term infant. This case emphasizes the importance of careful observation of all young infants who require surgery and anesthesia. This case has clinically important implications for patients scheduled for out-patient procedures because it is obvious that immaturity of the respiratory center is not limited to children with a history of prematurity, although the likelihood of such respiratory immaturity is inversely related to postconceptual age.<sup>5,¶</sup>

In conclusion, we suggest that neonates considered for surgery should ideally be the first case of the day so that the period of observation may be extended as long as is clinically indicated.<sup>15</sup> Although this is only one case in a full-term infant, it appears that abnormalities of respiration can be unmasked, just as in ex-premature infants, by the stress of surgery and/or administration of general anesthetic agents; such abnormalities will be most evident in the immediate postoperative period. Although our patient had a demonstrable abnormality of respiration, it would be premature to make specific recommendations regarding the management of all newborn patients as day surgical patients. We report this case to heighten the practitioner's awareness that such a problem may arise, albeit rarely; we are not suggesting that all infants be admitted to the hospital. The red flag in this case was persistent periodic breathing. If there is any question of abnormal breathing pattern in the infant, the infant should be admitted to the hospital for further observation of the respiratory pattern. Such infants should then undergo a more rigorous respiratory workup once the influences of

surgery and anesthesia have cleared. This infant may well represent a class of patients whose first episode of clinically apparent apnea is unmasked by anesthetic agents.

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## Recurrent Paralysis Following Piperacillin Administration

KEN MACKIE, M.D.,\* EDWARD G. PAVLIN, M.D.†

Several antibiotics have been shown to cause potentiation of the neuromuscular blockade produced by non-

depolarizing muscle relaxants.<sup>1</sup> Most clinical reports have involved the aminoglycosides, polymyxins, and clinda-

\* Resident in Anesthesiology.

† Associate Professor in Anesthesiology.

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Address reprint requests to Dr. Pavlin: Associate Professor, Department of Anesthesiology, Harborview Medical Center, 325 Ninth Avenue, Seattle, Washington 98104.

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