ANESTHESIOLOGY

Luck, an Inquisitive Mind, and Opportunities: Lessons Learned: A Blinded Study of Pulse Oximetry before It Became a Standard of Care

Charles J. Coté, M.D.

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A Single-blind Study of Pulse Oximetry in Children. By CJ Coté, EA Goldstein, MA Cote, DC Hoaglin, and JF Ryan. ANESTHESIOLOGY 1988; 68:184–8. Reprinted with permission.

Abstract

Oxygen saturation determined by pulse oximetry was monitored in 152 pediatric surgical patients divided into two groups. In one group, the oximeter data and alarms were available (N = 76) to the anesthesia team, and, in the other group, these data were unavailable (N = 76). A trained observer recorded all intraoperative hypoxic episodes and informed the anesthesia team of all major events (i.e., oxygen saturation 85% or less for 30 s or more; Pao2, approximately 52 mmHg). Thirty-five major events occurred: 24 in the unavailable group, and 11 in the available group ($P = 0.021$). A greater number of major events occurred in children 2 yr or younger ($P = 0.013$). Hypoxic events diagnosed by the oximeter, but not by the anesthesiologist, were more frequent in the unavailable group (13) than in the available group (5; $P = 0.0495$). American Society of Anesthesiologists (Schaumburg, Illinois) Physical Status III and IV patients were more likely to suffer a major event ($P = 0.009$ available, 0.006 unavailable). The pulse oximeter diagnosed hypoxemia before the signs and symptoms of hypoxemia were apparent (*i.e.*, before observed cyanosis or bradycardia). Major hypoxic events were unrelated to duration of anesthesia. Major events were evenly distributed among induction, maintenance, and awakening from anesthesia; a greater number of hypoxic events occurred during induction in the unavailable group ($P = 0.031$). No morbidity was documented in any patient who suffered a hypoxic event. More patients experienced borderline oxygenation in room air at the end of anesthesia (90% saturation or less) in the unavailable group (12 of 60) than in the available group (3 of 57; $P = 0.009$). The authors conclude that pulse oximetry, in contrast to changes in vital signs, does provide an early warning of developing hypoxemia in anesthetized children.

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As a junior faculty member, a young pup, you are always looking for your "niche"; once you find it, then you go for it. That niche may lead to a lifelong passion, significant clinical impact, and as a bonus, a promotion (fig. 1). It takes a bit of luck, an inquisitive mind, and recognition that an opportunity has arrived—the right place at the right time. This Classic Paper was the result of exploring clinical observations overlaid with discovery of my niche: improving patient safety.[1]

At a pivotal moment in my medical school training, I was caring for a critically ill preterm baby with hyaline membrane disease in the newborn nursery. Gregory *et al.*[2] published a method of providing positive end-expiratory pressure by administering high fresh gas flows into a loosely sealed Plexiglas box around the head; my attending refused to consider a medical student's suggestion, but the baby's pediatrician agreed it was worth a try, and the dying baby survived. This was a formative experience, which reinforced the principle that careful observation impacts patient outcomes; it also piqued my interest in anesthesiology and critical care.

After my pediatric residency, I changed to anesthesiology at the University of Pennsylvania (Philadelphia, Pennsylvania) and the Children's Hospital of Philadelphia (Philadelphia, Pennsylvania). During these impressionable years, I learned the excitement of studying and answering my clinical questions. In my third month of residency, I was providing neuroanesthesia to a patient, and after my attending had left the room, the surgeon requested mannitol. Unfamiliar with mannitol, I questioned the surgeon, who said to just "take a 50-ml syringe and give it." Thirty seconds later, the patient's blood pressure dropped to 70, and I stat paged my attending. Two years later, I observed the same transient yet reproducible response in a pediatric craniofacial procedure. At lunch the next day, I asked some attendings about this, and one suggested I should study it. During my 6-month fellow research block, I learned how to examine changes in organ blood flow with radiolabeled microspheres and found that this hypotensive response was the result of vasodilation in muscle. We examined this in humans on and off bypass and found that this effect was compensated with increased cardiac output when off bypass.[3] Our paper on this effect won first prize for the American Society of Anesthesiologists (ASA; Schaumburg, Illinois) Resident Research Award. I

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Charles J. Coté, M.D.: Department of Anesthesia, Critical Care and Pain Medicine, Harvard Medical School at the Massachusetts General Hospital for Children, Boston, Massachusetts.

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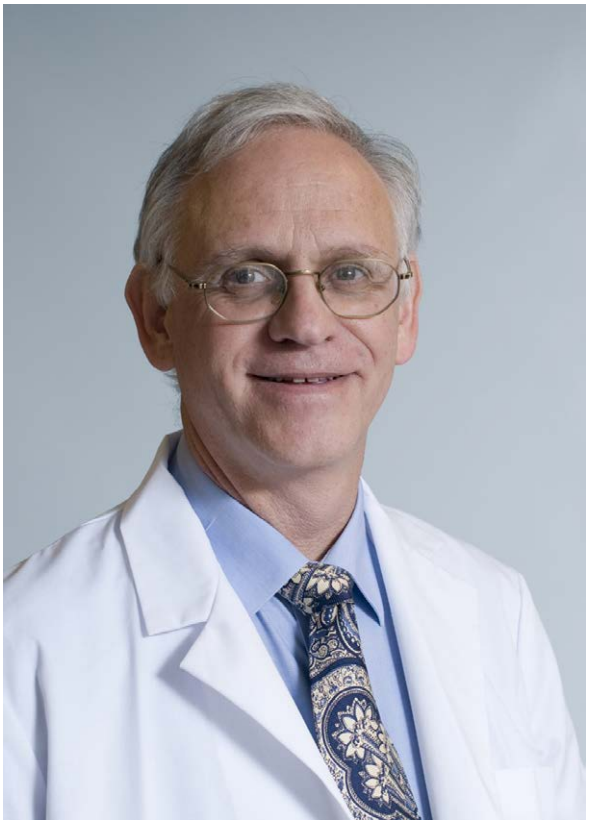

Fig. 1. Dr. Charles J. Coté.

was in the right place, with the right mentors who gave me the opportunity: Bryan E. Marshall, in whose laboratory I did my study; Eric Greenhow, who helped with statistics; and my chair, Jack Downes, who funded my research time. After I presented the abstract at the ASA, Richard Kitz, Chair of the Department of Anesthesia at Massachusetts General Hospital (Boston, Massachusetts), offered me a job on the spot—a job that I delayed due to my military obligation. Shortly after joining Massachusetts General Hospital, I was recruited to assist with ongoing studies by Nick Goudsouzian and others. My first day at the Shriners Burns Institute (Boston, Massachusetts) brought a case of cardiac electromechanical dissociation after a rapid administration of fresh frozen plasma. The child was successfully resuscitated with chest compressions and exogenous calcium. Our research group pursued several observations from this event that led to proving the equally rapid rise of ionized calcium after calcium chloride or calcium gluconate,[4] the lethality of citrate-induced hypocalcemia from fresh frozen plasma and halothane's calcium channel blockade,[5,6] and others.[7–9] Our success revealed the importance of the entire group being focused on clinical research and the academic support of our chair, Richard Kitz, and our division chief, John Ryan.

Five years earlier at the Children's Hospital of Philadelphia, a former preterm infant died during transport 2 h after inguinal hernia repair. With this fellowship case in mind, I proposed a prospective study of postoperative apnea in all children less than 1 yr of age at Massachusetts General Hospital and asked my colleague, Letty Liu, to take the lead.[10] We observed that preterm infants younger than 41 to 46 weeks postconceptual age were at risk for apnea. Ours was the first prospective study of this safety issue and the fruit of another clinical observation now taken to critical data collection that resulted in preliminary safety recommendations.[11]

In 1986, my emerging niche in patient safety coincided with an opportunity to attend the ASA annual meeting. I discovered a new company that claimed their device could provide continuous oxygen saturation monitoring. Nellcor (Pleasanton, California) was the first company to market pulse oximetry devices, and their clinical liaison educated me as to how it worked. I recognized its potential, and they lent me a first-generation device, the N100, to collect pediatric data. At that time, the first Harvard monitoring standards had been published, though oxygen saturation monitoring was not part of that document.[12] While the general culture of the Massachusetts General Hospital department under the leadership of Jeff Cooper and Dr. Kitz was patient safety, my colleagues were skeptical as I trialed the device. As was standard at the time, they relied upon clinical skills for observing cyanosis or other changes in vital signs. No other monitors such as transcutaneous oxygen monitors were available or reliable in the operating rooms.

The right place, right time, and opportunity struck again: I was ready to collect pediatric pulse oximetry data when I was approached by a pre-med college student, Andrew Goldstein, looking for a summer project. The study was a convenience sample of pediatric cases for which oximetry data were randomized to be either available or unavailable to the anesthesia team—the first blinded study of oximetry. Andrew collected continuous strip chart recordings and was instructed to notify the anesthesia team whenever the saturation was less than 85% for 30 s or longer. Minimal changes in vital signs (heart rate, blood pressure) were noted. The most striking observation was that all 14 patients described as cyanotic had saturations 72% or less (approximately 40 mmHg), and 9 patients with saturations less than 72% were described as noncyanotic! We drew the following conclusions: (1) nearly twice as many events occurred when the data were blinded; (2) ASA Physical Status III to IV patients had more events than I to II; (3) desaturation events occurred regardless of provider experience; (4) infants and toddlers are at greatest risk for desaturation; (5) the oximeter provided an early warning of developing events; and (6) we are

really bad at clinically diagnosing cyanosis, a fact known since 1947, when Comroe and Botelho measured various oxygen saturations in volunteers and concluded that "Visual impressions of cyanosis are unreliable"[13] (fig. 2). I suspect that our findings were used in part to support the later adoption of oximetry into the 1989 ASA monitoring standards.

During data collection, Andrew and I were reminded to never underestimate our powers of observation, no matter the level of training. One Monday, Andrew arrived with multiple colors of nail polish. "Dr Coté, I think I found something. Nail polish seems to affect the oximeter." We recorded room air saturations in volunteers with five nail polish colors. A blinded analysis concluded that blue and green, both of which absorb light in the same spectrum as the pulse oximeter (660 nm and 940 nm), produced lower readings; purple and red produced no effect; black's effect was minimal. Back on campus, Andrew later confirmed with spectrophotometry that the green and blue polishes we used absorbed light in those wave lengths;[14] this is now a board examination question.

Efforts to create monitoring standards in the late 1980s and the success of the pulse oximetry study reignited our group's interest in capnography, which was recommended but not mandated in the 1986 ASA monitoring standards. In a previous study of capnography,[15] we identified life-threatening events and even two cases of malignant hyperthermia.[16] Finding a common link with our oximetry study,[1] that young age equaled a greater risk of adverse airway events, we wondered, "What happens when we combine capnography and oximetry, or withhold one or the other or both from the anesthesia providers?"[17]

With data collection led by Norbert Rolf, an anesthesiologist, we obtained strip chart recordings of oximetry, electrocardiogram, and capnography. As in our previous study,[1] the oximeter provided the first indication of a developing desaturation event in most cases. Surprisingly, only a few (5 of 59) major desaturation events were diagnosed first by the capnograph (esophageal intubation, disconnects). Major capnography events were equivalent whether the monitor was available or unavailable (fig. 3). Refined from many details and observations, this study again yielded one major conclusion: infants 6 months and younger are the most vulnerable population and benefit most from continuous oximetry and capnography.[17] We also found that careful collection of physiologic data allowed for analysis of other problems: persistent cardiac arrhythmias associated with hypercarbia and halothane anesthesia,[18] increased frequency of desaturation events in children with upper respiratory infections,[19] and desaturation after rectal methohexital sedation.[20]

Interest in patient safety has persisted throughout my career. From the first edition of *A Practice of Anesthesia for Infants and Children* to the upcoming seventh edition,[21] I have viewed my textbook as a means of spreading the word regarding pediatric anesthesia safety issues. My portfolio of research, including my most recent study on continuous noninvasive cardiac output monitoring, is aimed at

TABLE 2. Distribution of Major Events by Age and Weight*

	Available		Unavailable		*p* Value
	Major Events	(N)	Major Events	(N)	
Age (yr)					
≤2	7	(33)	19	(32)	0.013
3–6	4	(23)	1	(23)	0.963
7–12	0	(16)	3	(16)	0.124
>12	0	(4)	1	(5)	0.545
Total	11	76	24	76	
Weight (kg)					
≤10	6	(23)	13	(21)	0.058
>10	5	(53)	11	(55)	0.120

* Some patients had more than one major event. This table excludes two patients with three major events; see Methods section.

Fig. 2. Major events by age and weight. From Coté *et al.* ANESTHESIOLOGY 1988.[1]

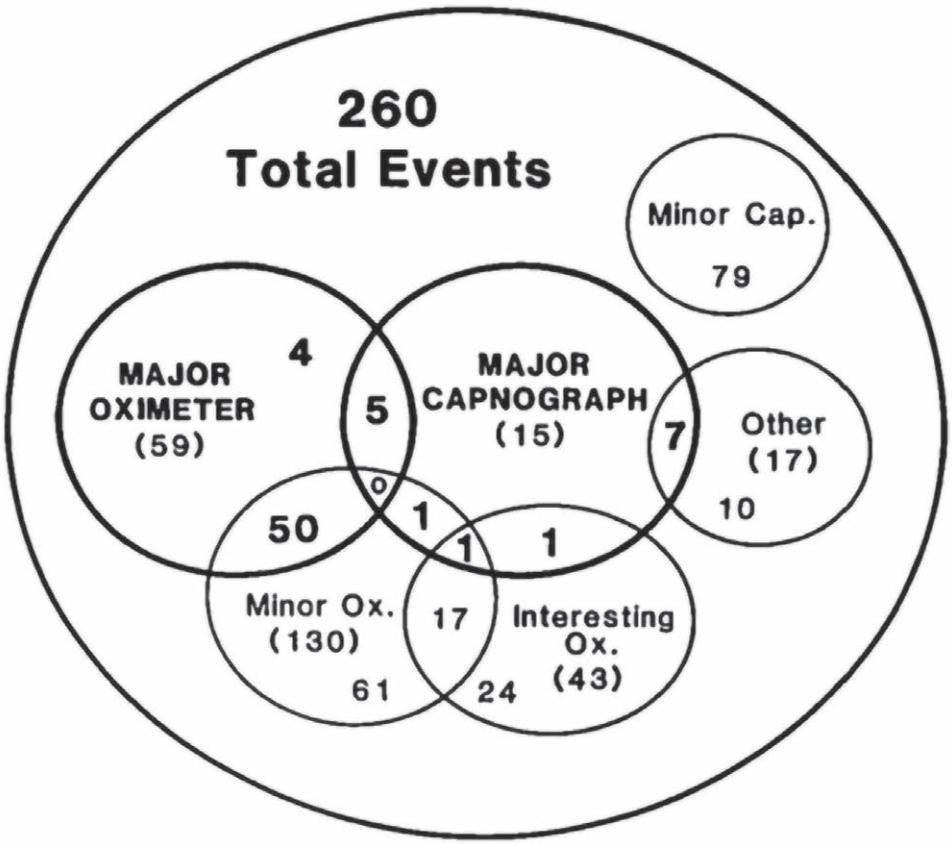

Fig. 3. Major desaturation events and major capnograph events. From Coté *et al.* ANESTHESIOLOGY 1991.[17]

improving patient safety.[22] As part of this study, my colleagues and I recorded oxygen saturation and once again found a strong relationship with desaturation events and age 6 months or younger.[23] As I look back, the incidence of desaturation events in infants 6 months or younger has not changed over the past 30-plus years despite advances in anesthetic agents and monitoring devices. Anyone caring for neonates and infants must anticipate that these events will occur at an increased frequency, regardless of how long we have practiced. There is an old phrase, "S____ happens," and there is little we can do to change this. But we *can* reduce potential morbidity; this is our raison d'être!

I conclude as I began: never doubt your powers of observation, and all research opportunities start with a good question. Enlist the help and participation of your colleagues, consult a statistician for proper study design before you begin data collection, and trust your instincts. It takes support from your chair, both financial aid and academic time, and full collaboration from your colleagues in order to collect a large body of patient data. I was blessed with wonderful mentors, role models, and colleagues, and lucky to be in the right place at the right time.

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Correspondence

Address correspondence to Dr. Coté: Department of Anesthesia, Critical Care, and Pain Medicine, Anesthesia; GRB444, 55 Fruit St., Boston, Massachusetts 02114. cote-cote@yahoo.com.

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