

RISKS: REVIEW ARTICLE

Cardiac arrest in anesthetized children: recent advances and challenges for the future

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Summary

Over the past 50 years the incidence of anesthesia-related cardiac arrest has declined, despite increased patient co-morbidities, the most significant determinant of anesthetic risk. Multiple factors have contributed to this improvement including safer anesthetic agents, better monitoring devices and the development of a specialized pediatric environment. Provider skill has benefitted from improved training and recognition of high-risk situations. Further improvements will depend on international, multispecialty efforts to standardize terminology and analyze large numbers of these infrequent adverse events.

Historical perspective

Several important features stand out from the last half-century of worldwide experience with anesthesia-related cardiac arrest. One is that the incidence of cardiac arrest in anesthetized children is higher than that in adults, as first reported in the seminal study of Beecher and Todd in 1954 (1). In this retrospective study of 10 university hospitals between 1948 and 1952, anesthesia was primarily responsible for cardiac arrest in 3.7 per 10 000 anesthetics, with a rate of 14 per 10 000 anesthetics in children 10 years of age or less. This difference in anesthesia cardiac arrest rates between children and adults has been reported many times since then (Table 1) (2–9).

An increased rate of anesthesia-related cardiac arrest in children under 1 year of age compared to older children has been reported (2,4–6,8). In two of these studies, children <1 month of age had the greatest risk of all (6,9). In the Pediatric Perioperative Cardiac Arrest (POCA) Registry, children under 1 month of age accounted for 24% of all cardiac arrests and had a mortality rate of 72%, the highest for any age group (10). Thus, it appears that within the pediatric popula-

tion, risk is inversely proportional to age, with newborns under 30 days at the highest risk.

Surgical site has also been described as a risk factor, with cardiac, vascular, and intra-abdominal procedures associated with the highest rates of cardiac arrest, particularly in newborns (2,6,8). Any relation between either age or surgical site and risk probably results in large measure from the impact of underlying patient disease. In Keenan's study, 20 of 27 arrests occurred in American Society of Anesthesiologists (ASA) physical status 3–5 patients (3). Tired (5) described an increasing incidence of serious complications as ASA physical status category increased (Table 2). In the POCA Registry, death following anesthesia-related cardiac arrest was predicted most strongly by ASA physical status, although emergency surgery was also predictive (Table 3) (7). When ASA physical status was accounted for, age alone was not predictive of death. In the newborn, significant underlying patient disease often takes the form of congenital anomalies such as congenital heart disease. Such children are not only more susceptible to anesthesia-related cardiac arrest but are more difficult to resuscitate once arrest has occurred.

Table 1 Summary table of studies of anesthesia-related cardiac arrest

Author	Country	Year	Definition anesthesia-related arrest	Age (years)	Cardiac arrests/10 000 anesthetics	Mortality/10 000 anesthetics	Common etiologies	
							Resp.	CV
Beecher (1)	US	1954	Directly responsible/ important contributor	<11 All	14 3.7			
Rachow (2)	US	1961	Same as Beecher	<1 1–12 >12	13.9 4.3 3.9	2.9 (all ages)	Anoxia aspiration	Anesthetic overdose
Keenan (3)	US	1985	Due solely	<12 >12	4.7 1.4	1.6	Failure to ventilate	Halothane overdose
Olsson (4)	Sweden	1988	Cannot be excluded as cause	<1 1–9	17 4.6	2.3 (all ages)	Hypoventilation	Halothane overdose
Tiret (5)	France	1988	Totally or partially	<1 1–14	19 2	0 0.3	Airway obstruction	Halothane anaphylaxis arrhythmia
Cohen (6)	Canada	1990	Not defined	<1 month <1 >1	28 12 3.5		Airway obstruct, laryngo-spasm	
Morray (7)	US	2000	Contribut in any way	0–18	1.4	0.36	Laryngo-spasm	Hypovolemia, blood loss
Braz (8)	Brazil	2006	Totally or partially	<1 month <1	28 12.7	0	Unable to intubate/ ventilate	
Flick (9)	US	2007	Attributed	0–18	0.65	0.21	Failure to intubate	Halothane, blood loss

Resp, respiratory; CV, cardiovascular.

Table 2 Relation between American Society of Anesthesiologists (ASA) physical status and the rate of complication⁵

ASA physical status	Rate of serious complications per 10 000 anesthetics*
1	4
2	34
3	116
4–5	164

* $P < 0.001$.

Another important historical feature of anesthesia-related cardiac arrest in children has been a decline in cardiac arrest rates since the report of Beecher and Todd (Table 1). In 1975, Smith reported a decline in the anesthesia-related mortality at the Children's Hospital in Boston from 2 per 10 000 anesthetics in the decade ending in 1966 to 0.6 per 10 000 anesthetics in the subsequent decade (11). Recently, the Mayo Clinic published a series of over 92 000 anesthetics administered to children over a 17-year period (9). The overall cardiac arrest rate was 2.9 per 10 000 anesthetics, with 0.65 per 10 000 attributable to anesthesia. Cardiac arrest rates of zero have been in reported from

Table 3 Multivariate analysis of predictors of mortality⁷

Factor	Odds ratio	95% confidence intervals	Estimated coefficient	P value
American Society of Anesthesiologists physical status 3–5	12.99	2.9–57.7	2.56	0.007
Emergency surgery	3.88	1.6–9.6	1.35	0.0036

outpatient settings when only ASA physical status 1 and 2 patients are considered (12,13).

By comparison, when anesthesia-related cardiac arrest rates in children <1 month and 1 month to 1 year of age are compared, little change has been seen over the same period (Table 1) (2,4–6,9). It may be that the severe comorbidities contributing to anesthesia-related risk in these age groups (e.g. congenital heart disease and other congenital anomalies) have prevented reductions in the incidence of arrest.

Along with a decline in rate of cardiac arrest has come a change in etiology (Table 1). Studies published prior to the 1980s emphasized complications from anesthetic overdose and from airway obstruction or aspiration from the lack of use or inappropriate use of endotracheal tubes. In the 1980s, respiratory

complications were more frequently due to inadequate ventilation because of unreversed muscle relaxants or to airway issues such as laryngospasm and complications of intubation. In the 1990s, a change from halothane to the newer agents such as sevoflurane resulted in a decline in arrests because of medication-related cardiovascular depression. A decrease in the relative frequency of respiratory events was also seen, probably from the introduction of pulse oximetry and capnography. Relatively more cardiovascular events were reported, frequently in children with cardiovascular disease (14). Arrests from hypovolemia because of blood loss have also become relatively more frequent (14).

Factors contributing to improved outcomes in pediatric anesthesia

Multiple factors are likely responsible for the decline in anesthesia-related cardiac arrest rates. These include improvements in anesthetic agents and monitoring devices, in the environment in which the anesthetic is given and in the education and training for the anesthesia provider.

Improved anesthetic agents

The POCA Registry has reported a decrease in medication-related arrests over the years of its existence (14), due at least in part to the declining use of halothane in pediatric anesthesia practice in favor of newer anesthetics, particularly sevoflurane. Sevoflurane has been reported to have less potential for producing bradycardia (15,16) and myocardial depression (17,18) in infants and children than does halothane. However, it is important to recognize that sevoflurane is also a cardiac depressant; reports of sevoflurane-related arrests have been submitted to the POCA Registry (14,19) as well as to others (8).

Anand *et al.* (20) demonstrated in neonates undergoing cardiac surgery that high dose, narcotic-based anesthesia suppresses physiologic stress responses better than lighter levels of inhalation-based techniques. Their high-dose narcotic technique was associated with reduced morbidity (metabolic acidosis, sepsis, and disseminated intravascular coagulation) and mortality. When this study was published in 1992, high-dose narcotic techniques were already considered the gold standard in pediatric cardiac anesthesia but Anand *et al.* provided a scientific basis for this approach. Subsequently, excellent outcomes have been reported from other institutions using a variety of narcotic-based techniques.

Advances in monitoring

Pulse oximetry and capnography are now routinely used in pediatric anesthesia and contribute to more rapid detection of problems with oxygenation and ventilation. Despite the fact that improved outcomes through the use of pulse oximetry have been difficult to prove, even with large prospective study designs (21), few doubt that oximetry serves as an important early warning device. In a single blind study of pulse oximetry in pediatric patients, Cote *et al.* demonstrated that the pulse oximeter frequently detects desaturation events prior to clinical recognition, even with experienced anesthesia personnel (22). The importance of pulse oximetry as an early warning device was also emphasized by the Australian Incident Monitoring Study, which reported that 85% of incidents were benefited by the use of oximetry (23). Capnography can provide the earliest diagnosis of potentially life threatening events such as accidental extubation, ventilator disconnects, or endotracheal tube obstruction, although subsequent pulse oximetry detection of desaturation provides a backup warning to the clinician. Capnography also reduces the incidence of hypercarbia and hypocarbia (24).

Evidence that pulse oximetry and capnography are having a positive impact on patient care comes from the changing profile of cardiac arrest in pediatric closed malpractice claims. In the 1970s, respiratory events resulted in the most liability in malpractice claims (25), whereas in the 1990s, claims for inadequate oxygenation and ventilation declined and claims for cardiovascular events became more frequent (26). The decrease in respiratory events may be attributable to prevention by oximetry and capnography.

The implementation of monitoring standards has been key in the universal adoption of these devices. The Harvard minimum monitoring standards were published in 1986 (27) based on the analysis of critical incidents (28). The ASA published similar standards simultaneously. Despite the dearth of evidence for improvement in outcomes, standards have led to a near-universal adoption of these devices.

Creation of the pediatric environment

The attainment of improved outcomes for children cared for in a specialized perioperative environment has several components. One is the effect of increased caseload on complications. In other specialties, improved outcome for a variety of high-risk procedures (e.g. congenital heart surgery, coronary artery surgery, and coronary angioplasty) has been positively

associated with caseload, presumably because competency improves with practice and experience. A similar phenomenon has been shown for the practice of pediatric anesthesia in France, leading to a recommendation of a minimum caseload of 200 pediatric anesthetics per year to reduce the incidence of complications (29). In addition to caseload, the creation of a specialized environment allows the coalescence of equipment and personnel dedicated to the care of children. In 1999, the American Academy of Pediatrics endorsed the concept of a specialized environment for provision of anesthetic care to children (30). These guidelines address operating room and recovery equipment, ancillary personnel and services, consultants, and services such as intensive care; they also serve to provide a comprehensive organization of services for the care of children, with the aim of providing improved outcomes (31).

Definition of the pediatric anesthesiologist

In the absence of a formal certification process, a widely accepted definition of the 'pediatric anesthesiologist' does not exist. Currently, therefore, the pediatric anesthesiologist is defined by some combination of specialized training and a clinical practice that is weighted toward care of the pediatric patient (32).

Initial training in pediatric anesthesia varies greatly from country to country. In 1997, the American Accreditation Council for Graduate Medical Education (ACGME) recognized fellowship training in pediatric anesthesiology (33). To become ACGME accredited, aspiring fellowship training programs must

demonstrate the provision of a full didactic curriculum, rich clinical exposure, and research training and mentoring for their trainees.

Continuing medical education is also important in providing safe care for children. Attendance at educational conferences and regular perusal of the medical literature keep the provider current with recent developments and trends and are necessary for hospital credentialing.

The presence of a pediatric anesthesiologist has been shown to improve outcomes. Keenan *et al.* reported that anesthetic outcomes for children, measured by the occurrence of cardiac arrest (34) or bradycardia (35), are improved when anesthesiologists trained or experienced in the care of children are involved. A study of pediatric anesthetic morbidity and mortality in the United Kingdom concluded with the statement: 'Surgeons and anesthesiologists should not undertake occasional pediatric practice' (36). The American Academy of Pediatrics has endorsed the concept that each medical staff define its scope of practice and create a credentialing process to acknowledge the increased risk involved in providing pediatric anesthetic and surgical care. Table 4 provides an example of a credentialing structure for institutions providing surgical care to children.

Regionalization of care is the byproduct of decisions to limit scope of practice. In the United Kingdom, transfer of emergency cases to regional centers has improved outcomes due in part to the level of expertise of providers (37). In France, organization of pediatric care according to age and degree of illness has been described, with emphasis on competencies of

Table 4 Example of a template for institutional credentialing of pediatric anesthesia providers

1. Scope of care for pediatric patients:	The institution should develop and maintain a written policy defining the types of pediatric patients that may receive perioperative care in the facility, based on risk assessment for children of various age groups, American Society of Anesthesiologists (ASA) classification, emergency status, and type of surgical procedure. Such a policy should take into account the training, experience, and availability of anesthesiologists, surgeons, pediatricians, nursing staff, and support personnel (laboratory, radiology, respiratory care, etc.)
2. Criteria for privileging:	The department of anesthesiology of each institution providing perioperative care for children should designate and categorize types of pediatric operative diagnostic and therapeutic procedures requiring anesthesia on an elective or emergency basis, with the goal of identifying patients at increased anesthetic risk. Suggested categories, with accompanying criteria, are as follows:
Regular Clinical Privileges:	Anesthesiologists providing and/or directly supervising clinical care for pediatric patients should be graduates of anesthesiology residency training programs accredited by the Accreditation Council for Graduate Medical Education (ACGME) or its equivalent. Such individuals should demonstrate competence in the care of pediatric patients, as determined by the department of anesthesiology.
Special Clinical Privileges:	In addition to the requirements noted above, anesthesiologists providing and/or directly supervising care of children designated as being at increased anesthetic risk (thus requiring special clinical privileges) should be graduates of ACGME-accredited pediatric anesthesiology fellowship training programs (or its equivalent) or have an equivalent amount of clinical experience. Such individuals should demonstrate competence in the care of high-risk pediatric patients, as determined by the department of anesthesiology.
The minimum annual case volume required in each category to maintain clinical competence should be stipulated by the department of anesthesiology, subject to approval by the facility's medical staff and governing board.	

practitioners, organization of services, and indications for transfer (38).

In the United States, despite guidelines for referral to pediatric surgical specialists (39), no system for regionalization of pediatric anesthesia exists other than the regional scattering of pediatric and university hospitals which are staffed with pediatric anesthesiologists. However, a variety of factors will likely contribute to increased regionalization. Performance-based credentialing will become more prevalent. A study in northern California suggested that in 85% of the region's hospitals, at best, one anesthesiologist would meet performance-based credentialing criteria of caring for at least one infant younger than 6 months of age per week (40). The majority of these institutions were within 50 miles of hospitals providing care for a larger number of infants per week. Cost will become an increasingly important factor. Hospitals may find that they cannot recoup the high costs of specialized care for a small number of patients and will favor transfer to regional centers. And finally, liability issues may play a role. Malpractice claims involving infants <6 months of age represent the single largest group, accounting for 20% of all pediatric claims (25).

Recognition of high-risk situations

The recognition of high-risk situations places the entire care delivery team on alert. It may, for example, influence the assignment of anesthesia provider and the choice of optimal time and location for surgical intervention in high-risk patients. As discussed earlier, young age, surgical type, significant underlying disease, and emergency surgery have been described as being associated with increased preoperative risk. Other situations or categories of patients that may be associated with increased risk include:

1. The former premature infant: In the early 1980s, a number of cases of apnea were reported following general anesthesia in infants born prematurely (37 weeks gestational age or younger) (41,42). A few of these cases included bradycardia, although none progressed to cardiac arrest. Reports of death in former premature infants following anesthesia and surgery are anecdotal and of unknown incidence. Increased incidence of postoperative apnea is associated with lower gestational and postconceptual age, a previous history of apnea (41) and anemia (42). Several strategies for prevention have been proposed. Elective surgery should be postponed if possible until after 55 weeks of postconceptual age, at which time the incidence of postoperative apnea is <1% (Figure 1) (43).

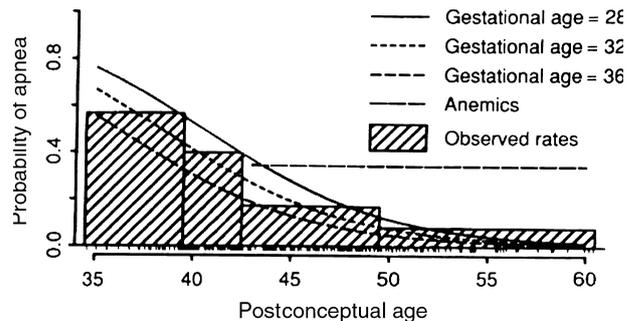


Figure 1 Probability of apnea for patients by gestational age and weeks postconceptual age. From Cote C, Zaslavsky A, Downes J *et al.* Postoperative apnea in former preterm infants after inguinal herniorrhaphy. *Anesthesiology* 1995; **82**: 809–822. (Figure 2, p 813).

Incidence of apnea may be lower following regional techniques without adjunctive sedation than after general anesthesia or regional anesthesia with intravenous sedation (44). Spinal anesthesia in infants has been shown to be both safe and effective (45). Administration of intravenous caffeine, $10 \text{ mg}\cdot\text{kg}^{-1}$, has been shown to decrease the incidence of postoperative apnea (46). Following anesthesia for children at risk for postoperative apnea, cardiorespiratory and pulse oximetry monitoring should be performed for 12–24 h; monitoring should be continued until at least 12 apnea-free hours have elapsed.

2. The irritable airway: The overall incidence of laryngospasm in children has been reported as 1–2%, with the highest incidence (2.8%) in children 0–3 months of age (47). The incidence of laryngospasm is also increased in children with upper respiratory infections, in children having airway surgery and in children being cared for by an inexperienced anesthesiologist (48). Generally, laryngospasm is treatable with positive airway pressure or a short acting muscle relaxant such as succinylcholine. Occasionally, however, laryngospasm results in severe hypoxemia and cardiac arrest. From 1994 to 2005, 17 such cases were reported to the POCA Registry (7,14). Of these, 15 occurred in children under 2 years of age. Six children had an upper respiratory infection. Ten arrests occurred during the induction of anesthesia. In eight of these arrests, no IV had been placed and intramuscular succinylcholine was required. These arrests occurred because of progressive hypoxia during the delayed onset of intramuscular succinylcholine. Seven arrests occurred during emergence from anesthesia, following extubation. In three of these cases, arrest occurred because of delayed

administration of muscle relaxant. Early placement of an IV catheter in children at risk for laryngospasm and early administration of intravenous succinylcholine following laryngospasm could have prevented cardiac arrest in many of these cases.

3. Hypovolemia from blood loss: From 1998 to 2004, 193 anesthesia-related arrests were reported to the POCA Registry (14). Cardiovascular causes of arrest accounted for the highest proportion of arrests (41% of total); among these, the most common identifiable single cause was hypovolemia related to blood loss (12% of all arrests). The majority of these arrests occurred during either spinal fusion or craniotomy/craniectomy. Anesthesia-related factors that contributed to hypovolemia-related arrest are shown in Table 5.

The anesthesiologist involved in these high-risk cases should carefully consider the use of invasive monitors and large bore peripheral intravenous catheters. Close attention must be paid to anticipating, estimating, and replacing blood loss.

The risk associated with transfusion must also be appreciated. Hyperkalemia from blood transfusion was another important cause of arrest reported to the POCA Registry (14). Hyperkalemia in this setting results from the administration of old blood, as potassium concentration in stored blood increases linearly with time. Irradiation dramatically accelerates the leakage of potassium from red cells into serum. The risk of hyperkalemia is highest in neonates or infants in whom one or

more blood volumes are transfused. Use of fresh red blood cells (rather than whole blood) and saline washing of irradiated cells may reduce the incidence of transfusion-associated hyperkalemia (49).

4. Heart disease: From 1994 through 2005, one-third of all arrests reported to the POCA Registry occurred in children with congenital or acquired heart disease (19). The most common category of heart disease lesion in patients suffering cardiac arrest was single ventricle (19% of all arrests). The highest mortality rates following arrest were seen in patients with aortic stenosis (62%) and cardiomyopathy (50%). Of the known mechanisms of cardiac arrest, myocardial ischemia was most common, usually because of hypotension in patients with aortic stenosis or cardiomyopathy or to pulmonary overcirculation in patients with single ventricle (prior to superior cavopulmonary anastomosis). Arrests occurred more frequently in the general operating room (54%) than in the cardiac operating room (26%) and the catheterization laboratory (17%) combined. Thus, children with high-risk lesions (such as those described earlier) should be considered high-risk patients regardless of the location or type of surgical procedure. This may include assignment of anesthesia personnel experienced in the management of such patients.
5. Placement of central venous pressure (CVP) catheters: The most common equipment-related cardiac arrests reported to the POCA Registry from 1994 to 2005 were because of complications of CVP catheter placement, usually in infants (19). Injuries from needle, guide wire, or catheter insertion resulted in pneumothorax, hemothorax, or hemo-pericardium. Many of these arrests may be preventable. The Closed Claims Project has reported that nearly half of the injuries because of CVP catheter insertion were potentially preventable with the use of ultrasound or pressure waveform monitoring (50). Verghese *et al.* have shown that ultrasound guidance of CVP catheter placement in children with congenital heart disease is superior to landmark guidance for reducing the incidence of complications (51).

Table 5 Anesthesia-related factors in cardiac arrests from hypovolemia because of blood loss reported to the Pediatric Perioperative Cardiac Arrest (POCA) Registry¹⁴

Anesthesia-related factor	% of hypovolemia-related arrests ^a
Underestimation of blood loss	48
Inadequate peripheral venous access	22
Central venous pressure catheter not present or not transduced	22
Arterial catheter not present or malfunctioning	17
Underestimation of pre-existing hypovolemia or anemia	13
Not enough help available to treat blood loss	13
Delay in getting blood from blood bank	13
Hypocalcemia not appreciated or undertreated	13
Development of coagulopathy	9

^aPercentages sum to >100% because of multiple factors in some cases.

Challenges for making and documenting future improvements

Lack of consistent definitions

Interpretation of outcomes data is made difficult by the lack of consistent definitions (52). For example, the definition of 'anesthesia related' varies from study to study (Table 1), from inclusive (e.g. even minor

contribution to arrest) to exclusive (e.g. solely causative, preventable human error) (53). Incidence calculations vary widely depending on this definition alone. Variation also exists in the time frame of perioperative adverse events (postanesthesia care unit discharge to 30 days), cause of arrest, and in the definition of 'preventable'. Comparing data from the many studies of the last few decades is difficult without a standardized set of definitions. It has even been suggested that improved outcomes for anesthetized patients over the last half-century are merely an artifact of the heterogeneity of definitions and methodology (54). An international effort, under the auspices of our national organizations, must be made to provide universally accepted terminology.

Dealing with low-incidence events

Improvement in quality of care is often measured by a reduction in the rate of adverse outcomes. However, adverse outcomes are relatively rare in anesthesia, making measurement of improvement difficult. For example, studies of the impact of monitoring standards (55) and the use of pulse oximetry (21) showed no statistical differences in outcome because of the statistical difficulties created by low-frequency events (56). One way of overcoming this problem is to focus on critical incidents or 'near misses' in addition to adverse outcomes. Because critical incidents are more common, measurement of their frequency may (or may not) serve as a proxy measure for adverse outcomes.

With the increased use of electronic anesthesia records, individual institutions have the opportunity to collect outcomes data over many years on even low-frequency events (2,6,9). However, single institutions may not be representative of the entire spectrum of pediatric care; thus, multi-institutional data repositories represent the future of outcomes analysis. Currently, the Society of Pediatric Anesthesia has initiated an outcomes data bank with 10 institutions from around the United States participating and plans for many more participants in the future. The development of multi-institutional data banks will not only provide useful insights into mechanisms of injury and preventive strategies, but will also encourage development of a common set of definitions that can be applied universally (52).

Breaking down specialty silos in outcomes analysis

When the data from the Beecher and Todd study are compared to recent data, anesthesia-only causes of mortality have improved 100-fold, but all-cause mortality has only declined 6.7-fold (57). This implies that future gains will occur by addressing areas of shared responsibility, including anesthesia-related factors, with our surgical, medicine, and nursing colleagues. Examples of areas ripe for such an analysis include surgical wound and blood stream infection, ventilator-associated pneumonia and transfusion of blood and blood products.

References

- Beecher H, Todd D. A study of the deaths associated with anesthesia and surgery. *Ann Surg* 1954; **140**: 2–35.
- Rachow H, Salantire E, Green LT. Frequency of cardiac arrest associated with anesthesia in infants and children. *Pediatrics* 1961; **28**: 697–704.
- Keenan RL, Boyan CP. Cardiac arrest due to anesthesia. A study of incidence and causes. *J Am Med Assoc* 1985; **253**: 2373–2377.
- Olsson G, Hallen B. Cardiac arrest during anesthesia. A computer-aided study in 250,543 anaesthetics. *Acta Anaesthesiol Scand* 1988; **32**: 653–664.
- Tiret L, Nivoche Y, Hatton F *et al.* Complications related to anaesthesia in infants and children. *Br J Anaesth* 1988; **61**: 263–269.
- Cohen MM, Cameron CB, Duncan PG. Pediatric anesthesia morbidity and mortality in the perioperative period. *Anesth Analg* 1990; **70**: 160–167.
- Morray J, Geiduschek J, Ramamoorthy C *et al.* Anesthesia-related cardiac arrest in children. *Anesthesiology* 2000; **93**: 6–14.
- Braz L, Braz JRC, Modolo NSP *et al.* Perioperative cardiac arrest and its mortality in children. A 9-year survey in a Brazilian tertiary teaching hospital. *Pediatr Anesth* 2006; **16**: 860–866.
- Flick RP, Sprung J, Harrison TE *et al.* Perioperative Cardiac Arrests in children between 1988 and 2005 at a tertiary referral center: a study of 92,881 patients. *Anesthesiology* 2007; **106**: 226–237.
- Morray J. Pediatric perioperative cardiac arrest registry: an update. *ASA News* 1996; **60**: 1–3.
- Smith R. The pediatric anesthetist, 1950–75. *Anesthesiology* 1975; **43**: 144–150.
- Petruscak J, Smith R, Breslin P. Mortality related to ophthalmological surgery. *Surv Anesthesiol* 1974; **18**: 87–95.
- Romano P. General anesthesia morbidity and mortality in eye surgery at children's hospitals. *J Pediatr Ophthalmol Strabismus* 1981; **18**: 17–21.
- Bhananker SM, Ramamoorthy C, Geiduschek JM *et al.* Anesthesia-related cardiac arrest in children: update from the pediatric perioperative cardiac arrest registry. *Anesth Analg* 2007; **105**: 344–350.
- Sarner JB, Levine M, Davis PJ *et al.* Clinical characteristics of sevoflurane in children. A comparison with halothane. *Anesthesiology* 1995; **82**: 38–46.
- Johannesson GP, Floren M, Lindahl SG. Sevoflurane for ENT surgery in children. A comparison with halothane. *Acta Anaesthesiol Scand* 1995; **39**: 546–550.
- Holtzman RS, van der Velde ME, Kaus SJ *et al.* Sevoflurane depresses myocardial contractility less than halothane during induction of anesthesia in children. *Anesthesiology* 1996; **85**: 1260–1267.
- Wodey E, Pladys P, Copin C *et al.* Comparative hemodynamic depression of sevoflurane versus halothane in infants: an

- echocardiographic study. *Anesthesiology* 1997; **87**: 795–800.
- 19 Ramamoorthy CR, Haberkern CM, Bhananker SM *et al.* Anesthesia-related cardiac arrest in children with heart disease: data from the pediatric perioperative cardiac arrest registry. *Anesth Analg* 2010; **110**: 376–382.
 - 20 Anand K, Hickey P. Halothane-morphine compared with high-dose sufentanil for anesthesia and post-operative analgesia in neonatal cardiac surgery. *N Engl J Med* 1992; **326**: 1–9.
 - 21 Moeller JT, Pedersen T, Rasmussen L. Randomized evaluation of pulse oximetry in 20,802 patients: I and II. *Anesthesiology* 1993; **78**: 436–453.
 - 22 Cote CJ, Goldstein EA, Cote MA *et al.* A single blind study of pulse oximetry in children. *Anesthesiology* 1988; **68**: 1184–1188.
 - 23 Runciman WB, Webb RK, Barker L. The Australian incident monitoring study. The pulse oximeter: applications and limitations—an analysis of 2000 incident reports. *Anesth Intensive Care* 1993; **21**: 543–550.
 - 24 Cote CJ, Rolf N, Liu LMP *et al.* A single-blind study of combined pulse oximetry and capnography in children. *Anesthesiology* 1991; **74**: 980–987.
 - 25 Morray JP, Geiduschek JM, Caplan RA *et al.* A comparison of pediatric and adult anesthesia closed malpractice claims. *Anesthesiology* 1993; **78**: 461–467.
 - 26 Jimenez N, Posner KL, Cheney FW *et al.* An update of pediatric anesthesia liability: a closed claims analysis. *Anesth Analg* 2007; **104**: 147–153.
 - 27 Eichhorn JH, Cooper JB, Cullen DJ *et al.* Standards for patient monitoring during anesthesia at Harvard Medical School. *J Am Med Assoc* 1986; **256**: 1017–1020.
 - 28 Cooper JB, Newbower RS, Kitz RJ. An analysis of major errors and equipment failures in anesthesia management: consideration for prevention and detection. *Anesthesiology* 1984; **60**: 34–42.
 - 29 Auroy Y, Ecoffey C, Messiah A *et al.* Relationship between complications of pediatric anesthesia and volume of pediatric anesthetics. *Anesth Analg* 1997; **84**: 234–235.
 - 30 American Academy of Pediatrics. Guidelines for the pediatric perioperative anesthesia environment. *Pediatrics* 1999; **103**: 512–515.
 - 31 Ecoffey C. Paediatric perioperative anaesthesia environment. *Curr Opin Anaesthesiol* 2000; **13**: 313–315.
 - 32 Morray J. Implications for subspecialty care of anesthetized children. *Anesthesiology* 1994; **80**: 969–971.
 - 33 Rockoff M, Hall S. Subspecialty training in pediatric anesthesia: what does it mean? *Anesth Analg* 1997; **85**: 1185–1187.
 - 34 Keenan RL, Shapiro JH, Dawson K. Frequency of anesthetic cardiac arrests in infants: effect of pediatric anesthesiologists. *J Clin Anesth* 1991; **3**: 433–437.
 - 35 Keenan RL, Shapiro JH, Kane FR *et al.* Bradycardia during anesthesia in infants: an epidemiologic study. *Anesthesiology* 1994; **80**: 976–982.
 - 36 Campling E, Devlin H, Lunn J. Report of the National Confidential Inquiry into Perioperative Deaths, London, 1990.
 - 37 McHugh G, Thoms G. Supervision and responsibility: the Royal College of anaesthetists national audit. *Br J Anaesth* 2005; **95**: 124–129.
 - 38 Courreges P, Ecoffey C. Regional organization for intensive care in children: need for maintenance of competence in paediatric anaesthesia and intensive care. *Ann Fr Anaesth Reanim* 2006; **25**: 445–450.
 - 39 American Academy of Pediatrics. Guidelines for referral to pediatric surgical specialists. *Pediatrics* 2002; **110**: 187–191.
 - 40 Hackel A, Macario A, Gregory GA *et al.* The demographics of inpatient pediatric anesthesia practice: implications for performance-based credentialing (PBC). *Anesthesiology* 1993; **79**: A1170.
 - 41 Liu L, Cote C, Goudsousian N *et al.* Life-threatening apnea in infants recovering from anesthesia. *Anesthesiology* 1983; **57**: 506–510.
 - 42 Welborn L, Hannallah R, Luban N *et al.* Anemia and postoperative apnea in former preterm infants. *Anesthesiology* 1991; **74**: 1003–1006.
 - 43 Cote C, Zaslavsky A, Downes J *et al.* Postoperative apnea in former preterm infants after inguinal herniorrhaphy: a combined analysis. *Anesthesiology* 1995; **82**: 809–821.
 - 44 Welborn L, Rice L, Hannallah R *et al.* Postoperative apnea in former preterm infants: prospective comparison of spinal and general anesthesia. *Anesthesiology* 1990; **72**: 838–842.
 - 45 Willams RK, Adams DC, Aladjena EV *et al.* The safety and efficacy of spinal anesthesia for surgery in infants: the Vermont Infant Spinal Registry. *Anesth Analg* 2006; **102**: 67–71.
 - 46 Welborn L, Hannallah R, Fink R *et al.* High-dose caffeine suppresses postoperative apnea in former preterm infants. *Anesthesiology* 1989; **71**: 347–349.
 - 47 Olsson G, Hallen B. Laryngospasm during anesthesia. A computer-aided study in 136,929 patients. *Acta Anaesthesiol Scand* 1984; **28**: 567–570.
 - 48 Schreiner M. Do children who experience laryngospasm have an increased risk of upper respiratory tract infection? *Anesthesiology* 1996; **85**: 475–482.
 - 49 Barcelona SL, Thompson A, Cote C. Intraoperative pediatric blood transfusion therapy: a review of common issues, Part I: hematologic and physiologic differences from adults; metabolic and infectious risks. *Pediatr Anesth* 2005; **15**: 716–726.
 - 50 Domino K, Spitellie P, Lee L *et al.* Injuries and liability related to central vascular catheters: a closed claims analysis. *Anesthesiology* 2004; **100**: 1411–1418.
 - 51 Verghese S, McGill W, Patel R *et al.* Ultrasound-guided internal jugular venous cannulation in infants: a prospective comparison with the traditional palpation method. *Anesthesiology* 1999; **91**: 71–77.
 - 52 Davis P. When assessing what we know we know is not enough: another perspective on pediatric outcomes. *Anesth Analg* 2007; **105**: 301–303.
 - 53 Morray J, Posner K. Pediatric perioperative cardiac arrest: in search of definitions. *Anesthesiology* 2007; **106**: 207–208.
 - 54 Lagasse R. Anesthesia safety: model or myth. *Anesthesiology* 2002; **97**: 1609–1617.
 - 55 Eichhorn J. Prevention of intraoperative anesthesia accidents and related severe injury through safety monitoring. *Anesthesiology* 1989; **70**: 572–577.
 - 56 Hanley J, Lippman-Hand A. If nothing goes wrong, is everything all right? Interpreting zero numerators *JAMA* 1983; **249**: 1743–1745.
 - 57 Roy R, Calicott R. Anesthesia practice models, perioperative risk and the future of anesthesiology. *ASA News* 2007; **71**: 14–17.