ANESTHESIA-RELATED CARDIAC ARREST IN CHILDREN

An Update

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INCIDENCE OF ANESTHESIA-RELATED CARDIAC ARREST

The improvement in mortality rates for anesthetized children over the past 50 years reflects the many improvements that have been made in pediatric perioperative care. The modern pediatric anesthesiologist is better trained than the predecessors of half a century ago, and has a vastly improved arsenal of monitoring devices and anesthetic agents from which to choose. The modern pediatric perioperative environment is better equipped to meet the unique needs of children. Techniques practiced by surgeons, nurses, radiologists and pharmacologists help create a far more sophisticated infrastructure than existed 50 years ago. Given these changes, it is not surprising that outcomes for patients have improved.

A higher incidence of mortality in anesthetized children compared with adults has been found many times since first reported in 1954 in the classic study of Beecher and Todd. In this retrospective study of ten university hospitals between 1948 and 1952, in nearly 600,000 anesthetics, anesthesia was primarily responsible for mortality in 3.7 per 10,000 anesthetic procedures, although the rate was 14 per 10,000 procedures for children 10 years of age or less.
In 1961, Rackow et al\textsuperscript{92} reported that the frequency of cardiac arrest associated with anesthesia in infants less than 1 year of age was 16.2 per 10,000 anesthetic procedures. This frequency was higher than that in children 1 to 12 years of age (6 per 10,000) and in adults (3.9 per 10,000). The difference between adults and children was significant only if children less than 1 year were included in the analysis. In other words, if there was a difference in mortality rate attributed to anesthesia between adults and children, it was primarily for children under 1 year of age.

The 1964 report from the Baltimore Anesthesia Study Committee\textsuperscript{45} found that the anesthesia-related mortality rate for children less than 15 years of age (3.3 per 10,000) was five times higher than that in teenagers or young adults. Anesthesia-related deaths represented a higher proportion of total deaths in neonates than in any other age group.

Clifton's study in 1963 from Sydney, Australia\textsuperscript{25} reported an incidence of anesthesia-related death in patients neonate to 20 years of age of 11.3 per 10,000 anesthetic procedures, twice as high as in patients 21 to 40 years of age. Most of the increase in mortality rate in the younger age patients was attributed to congenital heart disease.

In the past 20 years, anesthesia-related mortality in children has decreased considerably (Fig. 1). Smith\textsuperscript{104} reported a decline in the mortality rate at The Children's Hospital in Boston from two anesthesia-related deaths per 10,000 anesthetics for the decade ending in 1966 to 0.6 per 10,000 anesthetic procedures for the subsequent decade. A series of more than 35,000 consecutive tonsillectomies and adenoidectomies without any deaths, were reported from the Eye and Ear Hospital of Pittsburgh.

![Figure 1. Anesthesia-related mortality rates in children from studies published over the last 50 years; the year of publication is indicated by the author's last name.](image-url)
in 1974. Similarly, Romano reported 2186 ophthalmologic procedures without mortality. In a review of 8995 pediatric outpatient procedures from the Children’s National Medical Center in Washington, DC, there were no deaths. Larger series in the past decade from France, Canada, and the United States have reported anesthesia-related mortality rates of 0.2, 1.4, and 0.36 per 10,000 anesthetic procedures, respectively.

Despite advances in pediatric anesthesia, the anesthesia-related mortality rate in children is still higher than that in adults, and is higher in younger children than in older children. A number of studies have identified children under 1 year of age as being at the highest risk. In Tiret’s prospective survey of more than 40,000 anesthetic procedures from 440 French institutions, the risk of significant complications, including cardiac arrest, was significantly higher ($P<0.0001$) in infants less than 1 year of age (43 per 10,000) than in children over 1 year of age (5 per 10,000). In the Pediatric Perioperative Cardiac Arrest (POCA) Registry, patients under 1 year of age accounted for 55% of all anesthesia-related cardiac arrests. In Cohen’s study of nearly 30,000 anesthetic procedures from a single Canadian institution, children less than 1 month of age had the greatest risks of anesthesia-related major complications and deaths.

These studies suggest that risk of anesthesia-related cardiac arrest and death is inversely proportional to age, with the youngest patients at highest risk. Any relation between age and risk probably results in large measure from the impact of underlying patient disease, however. In Keenan and Boyan’s study in 1985, cardiac arrest occurred three times more often and death twice as often in the American Society of Anesthesiologist (ASA) Physical Status III or IV patients than in the ASA Physical Status I or II patients. In Tiret’s study, the relation between ASA Physical Status and rate of complications is shown in Table 1.

In the POCA study, death following anesthesia-related cardiac arrest was predicted most strongly by ASA Physical Status, though emergency surgery was also predictive (Table 2). When ASA Physical Status was accounted for, age alone was not predictive of death. In the newborn and infant, significant underlying patient disease usually takes the form of congenital anomalies, particularly congenital heart disease. Such chil-

<table>
<thead>
<tr>
<th>ASA Physical Status</th>
<th>Rate of Complications per 10,000 Anesthetics*</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>4</td>
</tr>
<tr>
<td>II</td>
<td>34</td>
</tr>
<tr>
<td>III</td>
<td>116</td>
</tr>
<tr>
<td>IV–V</td>
<td>164</td>
</tr>
</tbody>
</table>

*P <0.001

Table 2. MULTIVARIATE ANALYSIS OF PREDICTORS OF MORTALITY

<table>
<thead>
<tr>
<th>Factor</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>Estimated Coefficient</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA Physical Status</td>
<td>12.99</td>
<td>2.56</td>
<td>0.007</td>
<td></td>
</tr>
<tr>
<td>III-V</td>
<td>2.9–57.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergency Surgery</td>
<td>3.88</td>
<td>1.6–9.6</td>
<td>1.35</td>
<td>0.0036</td>
</tr>
</tbody>
</table>

ASA = American Society of Anesthesiologists


Children are not only more susceptible to anesthesia-related cardiac arrest, but are more difficult to resuscitate once arrest has occurred. The margin for error is less in a child with significant underlying disease.

Emergency surgery as a risk factor for anesthesia-related cardiac arrest in children has been described by multiple authors. The reasons for this increase in risk are unclear, though Keenan and Boyan speculated that an unprepared perioperative environment might be responsible.

The health care provider may also play a role in determining risk of anesthesia-related complications, including cardiac arrest. Keenan et al examined the incidence of cardiac arrest in patients 1 year of age or less during a 7-year period at a large university hospital. No patient cared for by a pediatric anesthesiologist, defined either by training or experience, had a cardiac arrest, whereas patients cared for by a nonpediatric anesthesiologist had an incidence of anesthesia-related cardiac arrest of 19.7 per 10,000 anesthetic procedures. In a subsequent study, the same authors found a lower incidence of bradycardia in children cared for by a pediatric anesthesiologist. In other subspecialties, such as congenital heart surgery, mortality rates are reduced in high-volume centers. The same is likely to be true for anesthesia.

CAUSES OF ANESTHESIA-RELATED CARDIAC ARREST

Along with a decline in the incidence of anesthesia-related cardiac arrest and death over the past 4 decades has come a change in the profile of causes of arrest. Studies published in the 1960s and 1970s emphasized a predominance of complications from airway obstruction or aspiration, often from the lack of use or inappropriate use of endotracheal tubes. In the past two decades, respiratory complications more often have been attributable to inadequate ventilation than to airway obstruction. In the 1990s, some investigators suggested a decline in the relative importance of respiratory versus cardiovascular causes of cardiac arrest. In the Closed Claims Project, the percentage of malpractice claims against anesthesiologists related to respiratory events...
declined during the 1990s compared with earlier decades. This change may correlate with the increased use of capnometry and pulse oximetry during that period; the relative frequency of respiratory events is higher in claims in which neither pulse oximetry nor capnometry is used compared with claims in which pulse oximetry and capnometry are used alone or in combination. Oximetry and capnometry may be better at detecting and therefore preventing respiratory events compared with cardiovascular events. Alternatively, the use of these monitors may result in some events being categorized as cardiovascular that otherwise would have been respiratory.

Also, in the past two decades, the relative frequency of cardiovascular events has increased. Many of the children in this category are less than 1 year of age and have congenital anomalies, particularly congenital heart disease.

Problems with medication administration are relatively more frequent; cardiovascular depression from the effect of inhaled anesthetics is a common cause of anesthetic-related cardiac arrest in several studies. Since 1994, the POCA Registry has been gathering information about cardiac arrest in children during anesthesia or recovery from anesthesia (Table 3). Medication-related events were the most common, accounting for 37% of all arrests. Cardiovascular depression from halothane, alone or in combination with other drugs, was responsible for two thirds of all medication-related arrests. One third of the patients in the POCA Registry were ASA Physical Status I or II; in this group, 64% of arrests were medication related (Fig. 2). Of the children who had cardiac arrests because of cardiovascular depression from halothane, 50% were 6 months of age or younger, and 50% had a reported inspired concentration of 2% or less. This finding is consistent with the observation that younger children may be vulnerable to cardiovascular depression from even conventional concentrations of halothane. Patients with significant underlying disease such as congenital heart disease may tolerate poorly any compromise in cardiac output caused by halothane-induced reductions in heart rate or myocardial contractility.

It remains unclear whether the increasing popularity of sevoflurane as an induction agent in children will have an impact on the number of reports of cardiac arrest attributed to inhalation agents. Sevoflurane is reported to have less potential for producing bradycardia and myocardial depression than halothane. The high cost of sevoflurane remains a significant disadvantage, particularly in the Third World.

TREATMENT OF CARDIAC ARREST IN THE OPERATING ROOM

The principles of cardiopulmonary resuscitation during the perioperative period follow the general guidelines established for the pediatric patient. There are some distinguishing characteristics of perioperative cardiac arrest that should result in better outcomes than are reported in
Table 3. MECHANISMS OF CARDIAC ARREST FROM THE PEDIATRIC PERIOPERATIVE CARDIAC ARREST REGISTRY

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication-related</td>
<td>55 (37%)</td>
</tr>
<tr>
<td>Inhalation agents</td>
<td></td>
</tr>
<tr>
<td>Halothane alone</td>
<td>26 (46%)</td>
</tr>
<tr>
<td>Halothane plus an intravenous medication</td>
<td>11 (20%)</td>
</tr>
<tr>
<td>Sevoflurane alone</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Intravenous medications</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>5 (9%)</td>
</tr>
<tr>
<td>Combination</td>
<td>5 (9%)</td>
</tr>
<tr>
<td>Intravenous injection of local anesthetic</td>
<td>5 (9%)</td>
</tr>
<tr>
<td>Succinylcholine-induced hyperkalemia</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>48 (32%)</td>
</tr>
<tr>
<td>Presumed CV, unclear etiology</td>
<td>18 (38%)</td>
</tr>
<tr>
<td>Hemorrhage, transfusion-related</td>
<td>8 (17%)</td>
</tr>
<tr>
<td>Inadequate or inappropriate fluid therapy</td>
<td>6 (13%)</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>5 (10%)</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Air embolism</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Pacemaker-related</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Vagal response</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Tetralogy hypercyanotic spell</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>30 (20%)</td>
</tr>
<tr>
<td>Laryngospasm</td>
<td>9 (30%)</td>
</tr>
<tr>
<td>Airway obstruction</td>
<td>8 (27%)</td>
</tr>
<tr>
<td>Difficult intubation</td>
<td>4 (13%)</td>
</tr>
<tr>
<td>Inadequate oxygenation</td>
<td>3 (10%)</td>
</tr>
<tr>
<td>Inadvertent extubation</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Presumed respiratory, unclear etiology</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Inadequate ventilation</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Bronchospasm</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Equipment-related</td>
<td>10 (7%)</td>
</tr>
<tr>
<td>Central line</td>
<td>4 (40%)</td>
</tr>
<tr>
<td>Breathing circuit</td>
<td>2 (20%)</td>
</tr>
<tr>
<td>Peripheral IV</td>
<td>1 (10%)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (30%)</td>
</tr>
<tr>
<td>Multiple events</td>
<td>5 (3%)</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>1 (&lt;1%)</td>
</tr>
<tr>
<td>Unclear etiology</td>
<td>1 (&lt;1%)</td>
</tr>
</tbody>
</table>

CV = cardiovascular


outpatient or (out-of-operating-room) inpatient cardiac arrest, however. Perioperative cardiac arrests occur under the watchful supervision of anesthesia personnel; as a result, intervention and resuscitation can begin immediately. Arrests caused by problems with oxygenation or ventilation, or cardiovascular depression from anesthetic agents, are often readily reversible, especially in the previously healthy patient. In addition, an adequate number of qualified personnel as well as resuscita-
Anesthetic Agents

The inhaled anesthetic agents, to varying degrees, are myocardial depressants. In the setting of cardiac arrest, successful resuscitation is more likely to occur if these agents are turned off as soon as cardiopulmonary arrest is diagnosed. The one exception to this rule is with hypertrophic myopathies, in which the presence of a negative inotropic agent may increase cardiac output. If patient awareness is a concern, amnestic agents can be judiciously administered once resuscitation has resulted in the return of circulation.
Airway Management

Endotracheal intubation is the optimal method of airway management and artificial ventilation during cardiopulmonary arrest. Though most patients who require cardiopulmonary resuscitation in the operating room are likely to be intubated at the time of arrest, this is not always the case. If it is not possible to intubate the patient’s trachea immediately, bag and mask ventilation should be performed to improve or maintain the patient’s oxygenation and ventilation. The efficacy of bag and mask ventilation has been demonstrated in Gausche’s study of out-of-hospital airway management. Children who were randomized to receive bag and mask ventilation until they reached the hospital had outcomes that were statistically identical to those children who were intubated in the field.

The laryngeal mask airway (LMA) was included in the most recent American Heart Association guidelines as an alternate airway management device. For health care providers not skilled in intubation techniques, it may be easier to learn to place an LMA. For most anesthesiologists, intubation skills are not required and the disadvantages of the LMA must be considered. Mechanical ventilation may not be feasible with an LMA, especially in the patient with noncompliant lungs. The risk of aspiration is unknown in the setting of cardiopulmonary resuscitation, but may be higher than with an endotracheal (ET) tube in place. Finally, the airway is not as secure with an LMA as with an ET tube, especially in the patient who requires transport. For airway management during cardiac arrest in the operating room, the LMA remains a backup technique for the child who cannot have an ET tube placed because of unfavorable anatomy.

Confirmation of tracheal placement of the ET tube is now required, using a qualitative or quantitative analysis of expired carbon dioxide (CO2) following a minimum of six breaths, and in the presence of a perfusing rhythm. A positive result confirms placement of the ET tube within the airway; a negative test indicates either esophageal intubation or airway intubation with poor or absent pulmonary blood flow. In the latter situation, an alternate means of confirmation of tube position is required.

The amount of CO2 present in expired gas correlates well with cardiac output (and therefore pulmonary blood flow) during cardiopulmonary resuscitation (CPR). This correlation may prove useful in several ways during CPR. A trend in end-tidal CO2 may help the resuscitator assess the impact of a change in therapy (e.g., a change in the rate, depth, or duration of chest compression) on cardiac output. In the high and low extremes, end-tidal CO2 values may provide some prognosticating ability. In one study, an end-tidal CO2 level of 10 mm Hg or less measured 20 minutes after the initiation of resuscitative efforts predicted death with 100% sensitivity and specificity.
Techniques of Chest Massage

Physiologic mechanisms for antegrade blood flow during chest compression have been widely debated and studied during the past four decades. At the time of Kouwenhoven’s report that rhythmic depressions of the sternum in animals produced pulsations in arterial pressure, it was assumed that anterior-to-posterior sternal depression selectively compressed the ventricles between the sternum and vertebrae, resulting in an artificial systole, with an increase in ventricular pressure, closure of the atrioventricular (A-V) valves, and antegrade ejection of blood.

More recently, a number of observations have cast doubt on this theory. Hemodynamic and angiographic studies show that chest compression causes a uniform increase in pressure in all intrathoracic cardiac structures. Because of competent venous valves, pressure is not transmitted to the extrathoracic veins, creating a pressure gradient for extrathoracic blood flow. This “thoracic pump” theory suggests that the heart functions as a passive conduit during CPR. The observation that the mitral valve remains open during sternal compression is supportive evidence of the thoracic pump theory (Fig. 3). Also supportive is Criley’s report of several patients who developed ventricular fibrillation during cardiac catheterization but could generate enough cardiac output to remain conscious by coughing repeatedly to increase intrathoracic pressure.

The thoracic pump theory has spawned a variety of resuscitative techniques to challenge the standard technique of sternal compression with interposed positive-pressure ventilation.

![Figure 3. Possible mechanisms for blood flow during CPR: the heart as a pump (left) and the thoracic pump (right). (From Scheien CL, Berkowitz ID, Traystman R, Rogers MC: Controversial issues in cardiopulmonary resuscitation. Anesthesiology 71:133–149, 1989; with permission.)](image-url)
Simultaneous Compression–Ventilation Cardiopulmonary Resuscitation

Ventilation is delivered simultaneously with chest compression to increase intrathoracic pressure and drive blood from the lungs. While studies in adult animals and humans have been promising, studies in infant piglets and small dogs show no advantages over standard CPR in systemic blood pressure or critical organ perfusion.12, 99

Interposed Abdominal Compression Cardiopulmonary Resuscitation

In addition to standard CPR, an additional rescuer performs abdominal compression prior to chest compression to “prime the pump” and provide retrograde flow to the cerebral and coronary arteries. Though studies have demonstrated improved cerebral and myocardial flow and improved oxygen uptake,52, 112 no study has shown an improvement in long-term outcome compared with standard techniques. Abdominal binding has also been studied for similar reasons. No increase in myocardial perfusion pressure has been seen, however.103 In addition, abdominal binding may cause a decrease in cerebral perfusion pressure.60

Active Compression–Decompression Cardiopulmonary Resuscitation

Using a suction cup device on the chest for decompression, the active compression–decompression technique has been shown in animals to increase cardiac output and organ perfusion compared with the standard technique21 and to maintain coronary blood flow in adult humans.102 Improved short-term survival, though not long-term survival, has been demonstrated in adults. Active compression–decompression is considered an optional technique in adults.5 There are no data in children on which to make a recommendation. The device is not yet commercially available in North America.

Results of these studies are not consistent and are often contradictory, largely because of differences in CPR models and compression techniques and differences in the maturity and chest wall geometry and compliance of the experimental subject. The preponderance of evidence is supportive of a thoracic pump mechanism, particularly in adults. The cardiac pump mechanism may be more operative in infants and children, however, in whom lower chest wall compliance may allow more direct cardiac compression than in adults. The American Heart Association guidelines for infants and children still support the standard technique.5 The revised recommendation for hand position at the lower half of the sternum corresponds to new understanding about the heart’s position in the thorax.85 This recommendation supports the heart-as-a-pump theory.

Two other techniques deserve mention. Open chest cardiac massage has been shown in animal116 and human37 studies to be associated with
better blood pressure and blood flow, although this may be less true in children than in adults. Other than for the child whose chest is already open at the time of arrest, in the absence of data showing a beneficial effect, the technique cannot be routinely recommended.

Success with extracorporeal membrane oxygenation as a rescue technique following congenital heart surgery has been reported. This technique may be an option for select patients centers with experience in this area.

Vascular Access

Successful resuscitation usually depends on reliable vascular access. A free-flowing peripheral IV may be all that is required. Resuscitation drugs, including epinephrine, calcium, sodium bicarbonate, glucose, and lidocaine, have very similar timings of onset and peak levels, whether administered peripherally or centrally (Fig. 4). Medications given through a peripheral intravenous (IV) line should be followed by a 5 mL to 10 mL saline flush to clear the catheter and push the medication into the central circulation.

If a central catheter is in place at the time of arrest, it should be used preferentially because of lower risk (compared with peripheral administration) of extravasation and tissue injury caused by vasoconstrictive agents such as epinephrine or sclerotic agents such as calcium. If a central line is not in place at the time of arrest and peripheral access cannot be obtained, the safest and easiest site to cannulate during resuscitative efforts is the femoral vein. Femoral venous pressure accurately reflects central venous pressure.

Because of high success rates with either peripheral or central ve-

![Figure 4](image-url)
Intraosseous cannulation in surgical patients, intraosseous needles are rarely used for perioperative resuscitation. Nonetheless, resuscitation carts in surgical suites should be stocked with styleted intraosseous needles, and personnel responsible for resuscitation should be familiar with their use (Fig. 5). Possible insertion sites include the anterior tibia, distal femur, medial malleolus, and anterior iliac spine. Prior to drug administration, it is important to confirm that a gravity drip runs easily to avoid extravasation and the potential for compartment syndrome. Other complications reported include tibial fracture, osteomyelitis, and microscopic pulmonary emboli (rarely of clinical significance). Any resuscitation drug that can be given intravenously can be given into the intraosseous space, with similar onset times and peak levels (see Fig. 4). It may even be possible to draw laboratory samples through an intraosseous needle.

The resuscitation drugs that can be delivered into the trachea are easily remembered by the pneumonic “LEAN”: Lidocaine, Epinephrine, Atropine, and Naloxone. Drugs that are not lipid soluble, such as sodium bicarbonate and calcium, can injure the trachea and should not be given through this route. Though clinical effects are seen following tracheal administration of epinephrine, drug absorption is variable and peak levels are blunted and delayed compared with the intravenous route. If the tracheal route is chosen, a dose 10 times the iv amount and diluted to 5 mL should be administered and followed by five manual ventilations.

**Intravascular Fluids**

A number of animal studies have reported that when hyperglycemia is produced prior to a cerebral ischemic event, neurologic outcome is
worse than in normoglycemic controls. The mechanism of this worsened outcome may be an increase in lactic acid production in the brain that aggravates neurologic injury. Alternatively, this may simply represent an epiphenomenon—i.e., hyperglycemia may reflect multiorgan system injury with impaired glucose use.

Current recommendations are to avoid glucose-containing solutions for initial fluid resuscitation in children, unless hypoglycemia is suspected or confirmed. Normal saline or Ringer’s lactate solution are preferred over colloidal solutions, because two meta-analyses suggest that albumin administration may be associated with increased mortality risks. Few of the patients in these studies were children, so it remains unclear whether or not these recommendations pertain to the pediatric population.

**Resuscitation Medications**

*Epinephrine*

In a series of experiments performed on dogs in the 1960s, Redding and Pearson showed that successful resuscitation depended on generating a diastolic blood pressure adequate to provide coronary perfusion; this was best achieved through the administration of α-adrenergic medications such as epinephrine. More recently, Michael et al showed that the effects of epinephrine during resuscitation result from selective vasoconstriction in noncerebral and nonmyocardial vascular beds. Studies comparing α-adrenergic agents have generally shown that both coronary and cerebral flows are related to the degree of blood pressure elevation produced.

The appropriate dose of epinephrine has been the subject of significant controversy and discussion. The current American Heart Association recommendation is 10 μg/kg administered as an intravenous bolus every 3 to 5 minutes, or 100 μg/kg through the endotracheal tube (in the absence of intravenous access). The dose of epinephrine needed to optimize blood flow to the brain and heart may be higher (100–200 μg/kg). Results in clinical trials of “high-dose” epinephrine have been inconsistent. In a nonblinded clinical trial in 20 children who did not respond to standard doses of epinephrine, high-dose epinephrine resulted in improved survival and neurologic outcomes compared with historical controls. In another uncontrolled pediatric study, however, a well-designed pediatric animal study, and multi-institutional adult studies, however, high-dose epinephrine failed to improve survival or neurologic outcome in survivors. High-dose epinephrine has been shown to induce cerebral vasoconstriction in a pig model of resuscitation from ventricular fibrillation. Other potential complications include a post-arrest hyperadrenergic state, with tachycardia, hypertension, ventricular ectopy, and myocardial dysfunction and necrosis. The current American Heart Association recommendation is that if the patient does not respond to a first dose of 10 μg/kg, higher doses (100–200 μg/kg)
may be considered, especially if diastolic blood pressure remains low (<20 mm Hg).5

**Vasopressin**

Vasopressin is an endogenous hormone that acts at specific receptors to mediate systemic vasoconstriction and reabsorption of water in the distal renal tubule, resulting in selective vasoconstriction in skin, skeletal muscle, intestine, and fat. Vasopressin was superior to epinephrine in a pig ventricular fibrillation model in maintaining coronary perfusion pressure necessary for defibrillation.120 In an uncontrolled study of infants and children with low blood pressure refractory to standard inotropic agents after cardiac surgery, vasopressin administration resulted in significant increases in blood pressure.96 In a pig model of asphyxial cardiac arrest, both epinephrine and vasopressin improved coronary perfusion pressure, but return of circulation and defibrillation rates were better in the animals given epinephrine.110 There are inadequate pediatric data at this time to make a recommendation concerning the routine use of vasopressin during cardiac arrest.

**Calcium**

Routine calcium administration does not improve the outcome of cardiac arrest. In addition, calcium may prevent reperfusion of the heart and brain, thereby worsening clinical outcome.24 Increased intracellular calcium concentrations can result in cell death. Currently, the only indications for calcium administration are documented or suspected hypocalcemia, hyperkalemia, hypermagnesemia, and calcium-channel blocker excess. Calcium is not indicated for electromechanical dissociation106 or asystole.107

**Magnesium**

Magnesium is a major intracellular cation and serves as a cofactor in more than 300 enzymatic reactions. It also can inhibit calcium channels. Indications for its use in cardiac arrest include documented hypomagnesemia and Torsades de pointes (polymorphic ventricular tachycardia). The usual recommended dose is 25 to 50 mg/kg, with a maximum dose of 2 g.

**Sodium Bicarbonate**

Routine administration of sodium bicarbonate during cardiac arrest has not been shown to improve outcome.70 Administration of sodium bicarbonate generates CO2; adequate minute ventilation and pulmonary blood flow are necessary to avoid respiratory acidosis. The intracellular acidosis from hypercapnea may diminish myocardial performance and preclude successful resuscitation.111 Arterial blood may not accurately
reflect the degree of respiratory acidosis present intracellularly and in mixed venous blood.\textsuperscript{115}

Once considered a first-line drug in the treatment of cardiac arrest, sodium bicarbonate is now recommended only for documented severe metabolic acidosis, or for the patient with prolonged cardiac arrest, once other measures have been taken to optimize ventilation and circulation. There is no absolute level of base deficit that requires treatment; both acuity and severity of acidosis must be taken into account when gauging therapy. Other indications for administration of sodium bicarbonate include hyperkalemia and hypermagnesemia. The usual dose is 1 mEq/kg IV or intra.

**Management of Arrhythmias**

Ventricular Fibrillation (VF) and Ventricular Tachycardia (VT): The algorithm for VF and VT has several important changes\textsuperscript{5} (Fig. 6). Bretylium has been dropped from the list of antiarrhythmic agents because of problems with hypotension and lack of documented efficacy.

Defibrillation with 2 to 4 joules/kg remains the mainstay of therapy for pulseless VT and VF. Newer defibrillators use biphasic waveforms that deliver current that first flows in a positive direction for a specified duration, then in a negative direction. Monophasic waveforms deliver current in the positive direction only, with a return to zero voltage either gradually (damped sinusoidal) or instantaneously (truncated exponential). In a variety of studies, biphasic shock appears to achieve the same defibrillation success rates as monophasic waveforms, but at significantly lower energy levels.\textsuperscript{36} Lower energy devices can be smaller, lighter and less expensive, with fewer maintenance requirements. All implantable defibrillators now employ biphasic waveforms.

Prospective data in children comparing monophasic with biphasic waveform external defibrillators are inadequate to draw conclusions. Currently, biphasic defibrillators are considered acceptable and useful alternatives to monophasic defibrillators for the treatment of pulseless VT or VF in children, though data are inadequate to recommend a biphasic energy dose.\textsuperscript{5} Automated external defibrillators either monophasic or biphasic, should not be used in children less than 8 years of age because the current delivered usually exceeds the recommended 2 to 4 J/kg.

Paddle size is selected to provide the largest surface area of paddle with the chest wall without contact between the paddles or electrodes. The larger the paddles, the lower the electrical impedance, and the higher the current flow. Infant paddles are recommended for children less than 10 kg, but larger paddles may be used if contact between the paddles is avoided.\textsuperscript{5}

Amiodarone is now an alternative to lidocaine as an antiarrhythmic agent (see Fig. 6) despite its long list of side effects, some of which are quite severe. Its inclusion in the recommendations is based on adult

Text continued on page 17
**Figure 6.** PALS algorithm for pulseless VT/VF, including use of amiodarone as the antiarrhythmic agent. (Adapted from the American Heart Association, Circulation 102: Circulation 11–1384, 2000, with permission.)
Amiodarone is a competitive inhibitor of both α- and β-adrenergic receptors,7 causing vasodilation and A–V node suppression. It also inhibits the outward potassium current, resulting in a prolongation of the QT interval123 and the inward sodium channels, thereby slowing ventricular conduction and prolonging QRS duration.75

In addition to its use in shock-resistant VT and VF, amiodarone is also recommended for use in junctional ectopic tachycardia93 and ectopic atrial tachycardia.41 The recommended loading dose for shock-resistant VT and VF is 5 mg/kg over several minutes to 1 hour,5 with repeated doses up to a maximum of 15 mg/kg.

Amiodarone has been adopted by the American Heart Association as a first-line agent in shock-resistant VT and VF despite its toxicity and its undesirable pharmacokinetic properties.75 The drug is highly protein bound in the plasma, and binds extensively with most tissues in the body, including the myocardium, liver, and lungs. As a result, time to antiarrhythmic effect is prolonged unless a loading dose is given. Terminal elimination half-life may exceed 100 days. One of the metabolites, desethylamiodarone, is electrophysiologically active. Amiodarone administration also increases serum concentrations of other drugs, including digoxin, flecainide, procainamide, and quinidine. Pharmacodynamic interactions with other drugs are numerous (Table 4). The most significant immediate side effect, hypotension, is a result of the antagonism of adrenergic receptors and calcium channels.100 Patients who are dependent on vasopressor infusions may be particularly vulnerable. Intravenous administration of calcium salts and vasopressors may be required to reverse the hypotensive effects of amiodarone. Other acute side effects include heart block, sinus bradycardia, and congestive heart failure. Complications associated with chronic use include pneumonitis and pulmonary fibrosis, hepatitis, renal dysfunction, and peripheral neuropathies.

**Bradycardia**

Bradycardia is the most rhythm frequently seen preceding cardiac arrest in children,79 and is caused by the effects of hypoxemia or the depressant properties of the anesthetic agent. In the POCA Registry,

<table>
<thead>
<tr>
<th>Drug(s)</th>
<th>Pharmacodynamic Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cathecholamines</td>
<td>α- and β-adrenergic antagonism</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>Sinus arrest and hypotension</td>
</tr>
<tr>
<td>Propranol</td>
<td>Bradycardia, sinus arrest</td>
</tr>
<tr>
<td>Quinidine</td>
<td>Torsades de pointes, ventricular tachycardia</td>
</tr>
</tbody>
</table>

epinephrine, alone or in combination with atropine, was the agent most commonly associated with a return of circulation. Atropine alone was frequently not sufficient. These findings are supportive of current guidelines for the approach to bradycardia. After ensuring adequate ventilation and oxygenation, epinephrine is the drug of choice. For suspected vagally mediated bradycardia, atropine is the drug of choice, in a dose of 0.02 mg/kg intravenous, with a minimum dose of 0.1 mg. In select cases of third-degree heart block, transthoracic pacing may be lifesaving.

**Supraventricular Tachycardia**

Chemical cardioversion with intravenous adenosine is now an alternative to electrical cardioversion, depending on whether or not intravenous access is present. Adenosine is an endogenous nucleoside that acts at specific receptors to cause temporary block of conduction through the A–V node. Its high degree of success in terminating supraventricular tachycardia is attributable to the interruption of re-entry circuits that involve the A-V node. Its short half-life of approximately 10 seconds results from metabolism by an enzyme that resides on the surface of red blood cells.

The recommended dose is 100 μg/kg (maximum dose 6 mg) as a rapid bolus injection followed by a 5-mL saline bolus through an IV site that is as close to the heart as possible. If there is no effect, the dose may be doubled (maximum dose 12 mg). Side effects are usually minor, though complete transient A–V block may occur, particularly in patients with underlying A–V node dysfunction. Temporary ventricular pacing may be required.

Verapamil is now discouraged for use in children with supraventricular tachycardia, and is contraindicated in infants, because of the risk of hypotension and myocardial depression. Amiodarone and procainamide can be used for supraventricular tachycardia, but not together, because extensive prolongation of the QT interval may occur.

**Preserving Neurologic Function**

Restoration and maintenance of adequate oxygen delivery are the keys to good neurologic outcome. If central nervous system depression is present following return of circulation, it is appropriate to leave the patient intubated and ventilated. Routine hyperventilation is no longer recommended, and may actually worsen the neurologic prognosis. Mild hypothermia of 33° to 36°C may have beneficial effects. There is not enough evidence to recommend active cooling of cardiac arrest survivors, but enough to recommend maintenance of mild hypothermia and avoidance of hyperthermia.
Stopping Resuscitative Efforts

In the absence of recurring VF or VT, toxic exposures, or significant hypothermia, resuscitative efforts may be stopped if there is no return of circulation despite full resuscitative efforts described in the current guidelines. Most survivors undergo CPR for 15 minutes or less; continuing CPR longer than 30 minutes usually does not produce additional benefits. Several studies have examined the correlation between epinephrine dosing and survival rates, and have found no survivors among those who required more than two doses of epinephrine. These studies were done in the wards or the emergency room, however, and outcomes may be better and prolonged efforts more justifiable for patients experiencing cardiac arrests in the operating room.

REDUCING RISK

Identifying High-Risk Factors

The identification of factors that have been associated with increased risk for anesthetized children may influence the assignment of anesthesia provider and the choice of optimal time and location for surgical intervention in the high-risk patient. As discussed, age of less than 1 year, significant underlying disease, and emergency surgery have been identified in multiple studies as being associated with increased perioperative risks. Other factors that may be associated with increased risks include:

The Premature or Expremature Infant

In the early 1980s, a number of cases of apnea were reported following general anesthesia in infants who had been born prematurely (37 weeks gestational age or younger). Apnea, defined as the cessation of breathing for longer than 15 to 20 seconds, or for a shorter duration if associated with bradycardia, is usually central in origin (cessation of respiratory effort), though mixed apnea (central and obstructive) has been reported. Postoperative apnea occurs more commonly in infants with a previous history of apnea and in those younger than 42 to 44 weeks postconceptual age, though apnea has been reported in expremature infants up to 55 weeks postconceptual age. The presence of anemia is another important risk factor.

Several strategies for prevention have been proposed. Elective surgery should be postponed until the child is beyond 55 weeks postconceptual age, at which time the incidence of postoperative apnea is less than 1%. Though apnea has been reported after general, spinal, and caudal anesthesia, one prospective series suggests that the incidence is lower following regional techniques without adjunctive sedation than after general anesthesia or regional anesthesia with IV sedation. Administra-
tion of iv caffeine, 10 mg/kg, has been shown to decrease the incidence of postoperative apnea. Following procedures on children at risk for postoperative apnea, cardiorespiratory and pulse oximetry monitoring should be performed for 12 to 24 hours; monitoring should be continued until at least 12 apnea-free hours have elapsed.

**Sedation**

Depression of respiratory drive and loss of cardiovascular tone have been reported with virtually every sedative and narcotic agent in use, including those believed to be benign, such as chloral hydrate. According to statistics compiled by the U.S. Department of Health and Human Services (DHHS), more than 80 deaths attributable to midazolam occurred within 3 years of its introduction in 1986. Seventy-eight percent of the deaths associated with midazolam were respiratory in nature, and in 57%, an opioid had also been administered. The combination of midazolam with fentanyl in doses within the recommended range has been demonstrated to produce hypoxemia and apnea in at least 50% of subjects. In the DHHS cases of midazolam-associated deaths, all but three occurred in patients unattended by anesthesia personnel.

The American Academy of Pediatrics became interested in sedation-related deaths when a series of children died in one dentist’s office in 1983. Shortly thereafter, the first guidelines of the American Academy of Pediatrics were published. These guidelines were revised in 1992. The important features of these guidelines include an adequate preprocedure evaluation and period of fasting, continuous monitoring of cardiorespiratory status, the presence of a trained health care provider, immediate availability of resuscitation equipment, and recovery and discharge criteria.

A recent survey of cardiac arrests during sedation in pediatric patients was compiled from reports of the U.S. Food and Drug Administration, the United States Pharmacopoeia, and a survey of physicians. Most of these mishaps were related to drug overdose, inadequate monitoring, inadequate skills of personnel administering drugs, or premature discharge. Outcome (52 deaths and six cases of permanent neurologic injury) was worse in cases of cardiac arrest outside the hospital compared with those inside. In both settings, the initial event was usually respiratory in nature. Cardiac arrest occurred as a secondary event more often in the non-hospital setting than in the hospital setting, however. This “failure to rescue” likely reflects a deficiency in the personnel or equipment necessary to recognize and treat airway and cardiovascular emergencies.

In Coté’s report, 28 of the deaths occurred after the American Academy of Pediatrics guidelines had been published. Such reports indicate the critical need for implementation and enforcement of sedation guidelines. In the United States, the Joint Commission on Accreditation of Healthcare Organizations mandates that the standard of care for sedated patients be standard throughout the hospital.
director of anesthesiology services must be responsible for establishing sedation guidelines, even in areas where non-anesthesiologists or non-physicians are responsible for administering sedative or narcotic medications and for monitoring the patient throughout the recovery phase.

Defining the Scope of Practice

In other subspecialties, such as congenital heart surgery, mortality rates are reduced in high-volume centers.46, 49, 53 The same is likely to be true for anesthesia. The steady decline in anesthesia-related morbidity and mortality rates over the past several decades has been attributed in part to better-trained and better-qualified physicians.50 Several studies claim that anesthetic outcomes for children, measured by the occurrence of cardiac arrest56 or bradycardia57 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 anaesthetists should not undertake occasional pediatric practice.”19 In contrast, it may be inappropriate and unnecessary to transfer the otherwise healthy child to a referral center for minor surgery. Perhaps the best solution to this dilemma is a compromise between a centralized and decentralized system of care. Patients defined as high risk (e.g., young age or severe underlying disease) would be transferred to a regional referral center, or cared for locally by a pediatric anesthesiologist. Some form of credentialing based on training or annual pediatric case load could be used to define pediatric anesthesiologist.

Providing the Appropriate Perioperative Environment for Children

Snyder was the first to report a series of anesthetic mishaps that were believed to have resulted from the use of adult equipment in children.105 Recently, the American Academy of Pediatrics endorsed the concept of a specialized environment for the provision of anesthetic care to children.4 The American Academy of Pediatrics guidelines include a requirement for specialized training, experience, and credentialing of personnel. Facility issues include pediatric equipment, drugs, and the necessary support services (e.g., nursing, pharmacy, laboratory, radiology, intensive care, and pain management). The responsibility for creating institutional guidelines rests with the hospital.

Adherence to Monitoring Standards

It makes sense that improved adherence to monitoring standards improve patients outcome. The fact that most anesthesia-related fatalities
involve human error\textsuperscript{29} suggests that monitoring devices are essential for patient safety even for the experienced, conscientious, and prudent anesthesiologist. The Pediatric Closed Claims analysis showed that 51\% of claims could potentially have been prevented with better monitoring.\textsuperscript{78} Pulse oximetry and capnography were used in only 7\% and 5\% of the Pediatric Closed Claims cases, respectively. Most anesthesiologists believe that the use of these monitors helps in the early identification of problems and allows intervention before a major mishap occurs,\textsuperscript{31, 33, 77} thereby lowering patient risks, improving outcomes, and lessening provider liability.

This belief is very difficult to prove statistically. Mishaps are rare in anesthesia, making measurement of improvement difficult.\textsuperscript{48} Eichhorn\textsuperscript{39} reviewed the anesthesia-related events during the years before and immediately after the adoption of minimum monitoring standards by the Harvard University teaching hospitals, and found no statistical differences in the two periods. In a study unlikely to be repeated, Moller et al\textsuperscript{77} performed a randomized evaluation of pulse oximetry in more than 20,000 patients and were able to show an increase in the number of episodes of desaturation, but no difference in outcome in the monitored group of patients.

Even without statistical proof, the anesthesia community believes that pulse oximetry and capnography are monitors that can improve quality of care and prevent anesthesia-related mishaps.\textsuperscript{40} Recently, the POCA Registry case analysis reported that pulse oximetry was used in 98\% of cases, and capnography in 86\%.\textsuperscript{79}

**Programs of Quality Improvement**

Quality improvement programs, by themselves, do not necessarily prevent patient injury. The Harvard Medical Practice Study, however, concluded that significant patient injury occurs because of medical management; one quarter of the injuries resulted from potentially preventable substandard care.\textsuperscript{14, 66} In the Pediatric Closed Claims study, care was judged substandard in 54\% of all claims.\textsuperscript{78} There is, therefore, the potential for quality improvement programs to reduce patient injury.

Bad outcomes may be caused by random errors, which are difficult to prevent, or to systematic errors, which should be controllable. Quality improvement is the process of continually evaluating anesthesia practice to identify systematic problems (opportunities for improvement) and implementing strategies to prevent their occurrence. Though a quality improvement program may focus on undesirable outcomes, the purpose is not to blame or identify “bad apples,” but to identify opportunities to improve the process or structure of care. Important characteristics of successful quality improvement programs include the following: (1) They are focused on system improvement rather than identification of individuals as outliers. (2) If they rely on self reporting, they are simple for the practitioner to complete healthcare to maximize compliance. (3)
They are context sensitive, such that patient disease and known surgical risks are taken into account in decisions about quality of care. (4) They include direct performance measures that reflect quality of care by assessing issues such as appropriateness, effectiveness, continuity of care, and patient satisfaction. Performance measures can be designed to address outcomes, processes, or even organizational structure. (5) They are continuous and self-generating.

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