2
Pediatric Cardiopulmonary Resuscitation

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Introduction 15
Definition of Pulseless Cardiac Arrest 15
Epidemiology of Pediatric Cardiac Arrest 15
The Phases of Cardiac Arrest and Cardiopulmonary Resuscitation 18
Is Cardiopulmonary Resuscitation Effective for Children? 19
Pediatric Ventricular Fibrillation 19
Interventions During the Low-Flow Phase: Cardiopulmonary Resuscitation 21
Postresuscitation Interventions 25
Neuropsychological Issues 26
Conclusion 26

Introduction

Infants and children are anatomically, physiologically, and developmentally different from adults. In contrast to adults, children infrequently suffer sudden ventricular fibrillation (VF) cardiac arrest from coronary artery disease. The pathogenesis of cardiac arrest and the most common rhythm disturbances are typically respiratory in children and cardiac in adults. In addition, the characteristics and outcomes of out-of-hospital versus in-hospital cardiac arrests are very different. In either setting, the causes of pediatric arrests are diverse and are usually secondary to profound hypoxia or asphyxia caused by respiratory or circulatory failure. Prolonged hypoxia and acidosis impair cardiac function and ultimately lead to cardiac arrest. By the time the arrest occurs, multiple critical organs of the body have generally suffered significant hypoxic–ischemic insults. Thus, prevention, intervention, approach, and procedures can differ for infants and children compared with adults.

Developmental changes affect cardiac and respiratory physiology before, during, and after cardiac arrest. As an example, newborn infants transitioning from amniotic fluid-filled lungs to gaseous breathing certainly differ from adolescents. Similarly, newborns and infants have much less cardiac and respiratory reserve and higher pulmonary vascular resistance than older children. In addition, many children who experience in-hospital cardiac arrest have preexisting developmental challenges and existing or evolving organ dysfunction. Normal developmental changes create challenges for outcome assessment across the age spectrum. These developmental changes and family relationships, unique to children, create special circumstances that can be anticipated and supported.

Definition of Pulseless Cardiac Arrest

Pulseless cardiac arrest is typically defined as the documented cessation of cardiac mechanical activity, determined by the absence of a palpable central pulse, unresponsiveness, and apnea. Separation of severe hypoxic–ischemic shock with poor perfusion from the nonpulsatile state of cardiac arrest can be challenging at any age. This separation can be especially difficult in neonates and infants because of their anatomic and physiologic differences. A rescuer's ability to determine cardiac arrest by a pulse check is neither sensitive nor specific in adults [1]. Not surprisingly, the pulse check is even more problematic in children. In adults, pulses can typically be palpated until the systolic pressure is <50 mm Hg. Because the normal systolic blood pressure in neonates is generally in the 60s, a decrease in blood pressure to *nonpalpable pulse* may occur earlier in the continuum from hypoxic–ischemic shock to nonpulsatile cardiac standstill. Furthermore, the best arterial pulse to palpate in an adult is the carotid pulse; however, the short, fleshy neck of a baby with potential to compress the airway and impede respiration limits the effectiveness of carotid pulse palpation in babies.

Epidemiology of Pediatric Cardiac Arrest

The epidemiology and evidence-based approach to pediatric cardiac arrest has been limited, in part, because of diverse disease processes and pathophysiology. Until recently, many pediatric studies *lumped* all pediatric cardiac arrests, such as those secondary to sudden respiratory failure (e.g., drowning, foreign body aspiration), progressive respiratory failure from infections and/or neuromuscular diseases, trauma, SIDS, septic shock, hypovolemic shock, anaphylaxis, primary cardiomyopathy, primary arrhythmia (e.g., VF or ventricular tachycardia [VT]), and drug intoxications, together. Such *lumping* of diverse etiologies of arrest makes analysis for incremental changes in outcomes attributable to individual interventions difficult. Characterization of the process of care and outcomes following pediatric cardiac arrest events has been limited by a lack of consistent data collection and analysis [2,3]. In particu-

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lar, pediatric reports often have not clearly differentiated among respiratory arrest, near-arrests (bradycardia with pulses) treated with cardiopulmonary resuscitation (CPR), and pulseless cardiac arrest [4]. In the early 1990s, international experts developed guidelines for uniform data reporting of out-of-hospital cardiac arrests and in-hospital resuscitation, the so-called Utstein style [2,4–6]. Nevertheless, epidemiologic information regarding pediatric cardiac arrests is dominated by retrospective chart reviews with small numbers and inconsistent definitions of cardiac arrest and CPR and a few small prospective single-center studies. Importantly, the quality of CPR is generally poor and not easily accounted for in most of these studies.

Pediatric In-Hospital Arrests

The true incidence of pediatric pulseless cardiac arrest is difficult to estimate as it is complicated by inconsistent definitions and assessment of pulselessness in children. Cardiac arrests were reported in 3% of children admitted to one children's hospital, in 1.8% of all children admitted to pediatric intensive care units (PICUs) in the United States [7], in 6% of children admitted to one PICU in Finland, and in 4% of children admitted to a pediatric cardiac intensive care unit [8]. Several well-designed in-hospital pediatric CPR investigations with long-term follow-up have established that pediatric CPR and advanced life support can be remarkably effective (Table 2.1). Almost two thirds of these cardiac arrest patients were initially successfully resuscitated (i.e., attained sustained return of spontaneous circulation [ROSC]). Most of these arrests/events occurred in PICUs and were caused by progressive life-threatening illnesses that had not responded to treatment despite critical care monitoring and supportive care. Almost three quarters of survivors to discharge have good neurologic outcome. The 1-year survival rates of 10%–44% are better than reported outcomes following out-of-hospital pediatric CPR.

Only a few studies have used the more rigorous Utstein style of reporting for in-hospital pediatric cardiac arrests and CPR [9]. Two describe all CPR events at children's hospitals in Brazil [10] and Finland [11]. The most common causes of the events were progressive respiratory failure and progressive shock. Approximately two thirds of the children attained sustained ROSC, and 1-year survival was 15% and 18%, respectively.

Recently published Utstein-style reports of in-hospital pediatric cardiac arrests are derived from the American Heart Association's multicenter National Registry of Cardiopulmonary Resuscitation (NRCPR) (http://www.nrcpr.org/). The NRCPR is a prospective, multicenter observational registry of in-hospital cardiac arrests and resuscitations. The large size, scope, and quality of the NRCPR distinguish this North American database characterizing the process and outcome of pediatric in-hospital CPR events. These important characteristics are summarized in Tables 2.2 and 2.3.

In these NRCPR reports, a cardiac arrest was explicitly defined as pulseless (cessation of cardiac mechanical activity), determined by the absence of a reported palpable central pulse, unresponsiveness, and apnea. Events were excluded if the cardiac arrest began out of hospital, involved a newly born in a delivery room or neonatal intensive care unit, or was limited to a shock by an implanted cardioverter-defibrillator. Most of these arrests occurred in children with progressive respiratory insufficiency and/or progressive circulatory shock [13]. These children often had progressive underlying critical illnesses despite aggressive critical care monitoring and therapy. Therefore, 95% of these arrests were witnessed and/or monitored, and only 14% occurred on a general pediatric ward. Before the arrest, 57% of these children were mechanically ventilated, 38% had continuous vasopressor infusions, and 29% had continuous direct arterial blood pressure monitoring.

Despite the diverse and complex clinical circumstances leading to their arrests, 52% attained sustained ROSC, 36% survived for 24 hours, and 27% survived to hospital discharge. Outcomes for these children were substantially better than reported outcomes for adults in this registry (adjusted odds ratio, 2.3 [95% confidence limit 2.0–2.7]). Importantly, 65% of these children had good neurologic outcome, defined as: (1) Pediatric Cerebral Performance Category of 1, 2, or 3 or (2) no change from baseline Pediatric Cerebral Performance Category [13]. Of importance, 200 children who received chest compressions without pulselessness during this same observation period were excluded from the NRPCR cardiac arrest analysis because they did not ever completely lose their pulse during the event. Similar to the two previous Utstein-style

Table 2.1. Summary of representative studies of outcome following in-hospital pediatric cardiac arrest.

First author, year	Setting	No. of patients	ROSC	Survival to discharge	Good neurologic survival
Samson, 2006, NRCPR [12]	In-hospital CA, (initial VF/VT rhythm)	272 (104)	(70%)	(35%)	(33%)
Nadkarni, 2006, NRCPR [13]	In-hospital CA	880	459 (52%)	236 (27%)	154 (18%)
Reis, 2002 [10]	In-hospital CA	129	83 (64%)	21 (16%)	19 (15%)
Extracorporeal Life Support Organization, 2002 [unpublished]	In-hospital CA resuscitation by ECMO	232	N/A, all needed ECMO	88 (38%)	NR
Suominen 2000 [11]	In-hospital CA	118	74 (63%)	1-year survival, 21 (18%)	NR
Parra 2000 [14]	Pediatric cardiac ICU CA	32	24 (63%)	14 (44%)	8 (25%)
Chamnanvanakij, 2000 [15]	In-hospital intubated neonatal ICU patient with chest compressions for bradycardia	39	33 (85%)	CPR, 20 (51%) CA, 10%	CPR 5 (13%) (6 lost to follow-up)
Slonim, 1997 [7]	In-hospital pediatric ICU CA	205	NR	28 (14%)	NR
Torres, 1997 [16]	In-hospital CA	92	NR	1-year survival, 9 (10%)	7 (8%)
Zaritsky, 1987 [17]	In-hospital CA	CA 53	NR	CA, 5 (9%)	NR
Young, 1999 [unpublished]	Meta-analysis, in-hospital CA	544	NR	129 (24%)	NR
Lopez-Herce, 2005 [18,19]	Mixed in-hospital and OOH CA	213	110 (52%)	45 (21%)	34 (16%)
Tunstall-Pedoe, 1992 [20]	Mixed in-hospital and OOH CA	3,765	1,411 (38%)	706 (19%)	NR

Note: CA, cardiac arrest; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; OOH, out of hospital; NR, not reported; NRCPR, National Registry of Cardiopulmonary Resuscitation; ROSC, return of spontaneous circulation; VF, ventricular fibrillation; VT, ventricular tachycardia.

Table 2.2. Characteristics of pediatric in-hospital cardiac arrests from the American Heart Association's National Registry of Cardiopulmonary Resuscitation.

Characteristic	Pediatric cardiac arrest n = 880 (100%)
Age (years)	
Mean (SD)	5.6 (6.4)
Median (range)	1.8 (0–17.0)
Sex	
Male	473 (54)
Female	407 (46)
Race/ethnicity	
White	447 (51)
Black	226 (26)
Hispanic	105 (12)
Other/unknown	102 (12)
Patient type	
In-patient	750 (85)
Emergency department	121 (14)
Other (outpatient, visitor, or employee)	9 (1)
Illness category	
Medical, cardiac	158 (18)
Medical, noncardiac	402 (46)
Surgical, cardiac	150 (17)
Surgical, noncardiac	62 (7)
Trauma	91 (10)
Other[†]	17 (2)
Preexisting conditions	
Respiratory insufficiency	511 (58)
Hypotension/hypoperfusion	319 (36)
Congestive heart failure	273 (31)
Pneumonia/septicemia/other infection	259 (29)
Arrhythmia	182 (21)
Renal insufficiency	104 (12)
Diabetes mellitus	11 (1)
Metabolic/electrolyte abnormality	178 (20)
Baseline depression in CNS function	151 (17)
Metastatic or hematologic malignancy	43 (5)
Myocardial infarction	21 (2)
None[‡]	69 (8)
Hepatic insufficiency	55 (6)
Acute CNS nonstroke event	94 (11)
Acute Stroke	5 (1)
Major Trauma	97 (11)
Toxicologic problem	12 (1)

Source: Adapted from Nadkarni et al. [13].

pediatric in-hospital studies, only 82% of children who received chest compressions fit the definition of pulseless cardiac arrest. As expected, children who received chest compressions for bradycardia with pulses had a much higher survival to hospital discharge rate (60%) than those with pulseless cardiac arrest (27%, $p < 0.001$) [13].

Pediatric Out-of-Hospital Arrests

Outcomes following pediatric out-of-hospital arrests appear to be worse than after in-hospital arrests (Table 2.4). In particular, neurologic outcomes appear to be much worse among children who are out-of-hospital arrest survivors. Two diseases have especially poor outcomes: traumatic arrests and SIDS. Traumatic cardiac arrests typically result from either airway compromise and severe, prolonged hypoxia or exsanguination resulting in profound circulatory shock. Not surprisingly, chest compressions with an inadequately filled heart are not likely to provide adequate coronary and cerebral perfusion. Sudden infant death syndrome patients are typically discovered a long time before resuscitation is attempted, with understandably poor outcome. In most series of out-of-hospital pediatric cardiac arrests, more than one third of the children have the diagnosis of SIDS. For other pediatric cardiac arrests in the prehospital setting, CPR and advanced life support from emergency medical service (EMS) providers may be applied very late, after profound hypoxia and hypoperfusion of vital organs. Not surprisingly, these poor outcomes after pediatric out-of-hospital cardiac arrests are similar to the poor outcomes after adult non-VF out-of-hospital cardiac arrests.

Table 2.3. Event characteristics of pediatric in-hospital cardiac arrests from the American Heart Association's National Registry of Cardiopulmonary Resuscitation.

Characteristic	Pediatric cardiac arrest (n = 880)
Event location	
Intensive care unit	570 (65%)
Emergency department	116 (13%)
General inpatient	123 (14%)
Diagnostic area	21 (2%)
Outpatient, other, or unknown	20 (2%)
Operating room or PACU	30 (3%)
First-documented pulseless rhythm	
Asystole	350 (40%)
VF and pulseless VT	120 (14%)
VF	71 (8%)
Pulseless VT	49 (6%)
PEA	213 (24%)
Unknown by documentation	197 (22%)
Discovery status at time of event[†]	
Witnessed and/or monitored	834 (95%)
Witnessed and monitored	727 (83%)
Witnessed and not monitored	73 (8%)
Monitored and not witnessed	34 (4%)
Not monitored and not witnessed	46 (5%)
Immediate cause(s) of event	
Arrhythmia	392 (49%)
Acute respiratory insufficiency	455 (57%)
Hypotension	483 (61%)
Acute myocardial infarction or ischemia	12 (2%)
Metabolic/electrolyte disturbance	95 (12%)
Acute pulmonary edema	33 (4%)
Acute pulmonary embolism	6 (1%)
Airway obstruction	41 (5%)
Toxicologic problem	9 (1%)

Note: PACU, postanesthesia care unit; PEA, pulseless electrical activity; VF, = ventricular fibrillation; VT, ventricular tachycardia.
Data are expressed as absolute number (percentage); percentages may not all total 100 because of rounding.
Source: Adapted from Nadkarni et al. [13].

Table 2.4. Summary of representative studies of outcome following out-of-hospital pediatric cardiac arrest.

First author, year	Setting	No. of patients	ROSC	Survival to discharge	Good neurologic survival
Gerein, 2006 [21]	OOH CA, Canada	503	25 (5%)	9 (2%)	NR
Donoghue, 2005 [22]	OOH CA, systematic review	5,363	165/594 (27.8%)	647/5,363 (12.1%)	131/3,272 (4.0)
Young, 1999 [unpublished]	Meta-analysis, OOH CA	1,568	NR	132 (8%)	NR
Sirbaugh, 1999 [23]	OOH CA	300	33 (11%)	6 (2%)	1 (<1%)
Suominen, 1998 [24]	OOH CA, after trauma	41	10 (24%)	3 (7%)	2 (5%)
Suominen, 1997 [25]	OOH CA	50	13 (26%)	8 (16%)	6 (12%)
Schindler, 1996 [26]	OOH CA	80	43 (54%)	6 (8%)	0 (0%)
Kuisma, 1995 [27]	OOH CA	34	10 (29%)	5 (15%)	4 (12%)
Dieckmann, 1995 [28]	OOH CA	65	3 (5%)	2 (3%)	1 (1.5%)
Lopez-Herce, 2005 [18,19]	Mixed in-hospital and OOH CA	213	110 (52%)	45 (21%)	34 (16%)
Tunstall-Pedoe, 1992 [20]	Mixed in-hospital and OOH CA	3,765	1,411 (38%)	706 (19%)	NR

Note: CA, cardiac arrest; OOH, out of hospital; NR, not reported; ROSC, return of spontaneous circulation.

The Phases of Cardiac Arrest and Cardiopulmonary Resuscitation

There are at least four phases of cardiac arrest: (1) *prearrest*, (2) *no flow* (untreated cardiac arrest), (3) *low flow* (CPR), and (4) *postresuscitation* [29]. Interventions to improve outcome from pediatric cardiac arrest should be targeted to optimize therapies according to the timing, duration, intensity, and *phase* of resuscitation as suggested in Table 2.5. The prearrest phase represents the largest potential opportunity to impact patient survival by preventing pulseless cardiopulmonary arrest. Interventions during the prearrest phase focus on prevention. Infant safety seats and safe driving to prevent traumatic arrests, water safety programs to prevent drowning arrests, and medication safety caps to prevent drug poisoning arrests are well-known highly effective efforts to prevent cardiac arrests. Medical emergency teams (rapid response teams) are being trained to recognize and intervene when cardiac arrest is impending. Because many pediatric cardiac arrests are caused by progressive respiratory failure and shock, the main focus of the Pediatric Advanced Life Support (PALS) is the early recognition and treatment of respiratory failure and shock in children (i.e., prevention of cardiac arrest in the prearrest phase).

Interventions during the *no-flow* phase of untreated pulseless cardiac arrest focus on early recognition of cardiac arrest and beginning initiation of basic and advanced life support [30]. When there is insufficient oxygen delivery to the brain or heart, CPR should be started. The goal of effective CPR is to optimize coronary perfusion pressure and blood flow to critical organs during the *low-flow* phase [31]. Basic life support provided by continuous, effective chest compressions (characterized by push hard, push fast, allow full chest recoil, minimize interruptions, and do not overventilate) is the emphasis in this phase.

The *postresuscitation* phase is a high-risk period for brain injury, ventricular arrhythmias, and other reperfusion injuries. Injured cells can hibernate, die, or partially or fully recover function. Overventilation (hyperventilation) is frequent and can have adverse effects during and following CPR [32]. Interventions such as systemic hypothermia during the immediate postresuscitation phase strive to minimize reperfusion injury and support cellular recovery [33,34]. The postarrest phase may have the most potential for innovative advances in the understanding of cell injury and death, inflammation, apoptosis, and hibernation, ultimately leading to novel interventions. Thoughtful attention to management of temperature, glucose, blood pressures, coagulation, and optimal ventilation may be particularly important in this phase. The rehabilitation stage of postresuscitation concentrates on salvage of injured cells, recruitment of hibernating cells, and reengineering of reflex and voluntary communications of these cell and organ systems to improve functional outcome.

The specific phase of resuscitation should dictate the timing, intensity, duration, and focus of interventions. Emerging data suggest that interventions that can improve short-term outcome during one phase may be deleterious during another. For instance, intense vasoconstriction during the low-flow phase of cardiac arrest may improve coronary perfusion pressure and probability of

Table 2.5. Phases of cardiac arrest and resuscitation.

Phase	Interventions
Prearrest phase (protect)	• Optimize community education regarding child safety • Optimize patient monitoring and rapid emergency response • Recognize and treat respiratory failure and/or shock to prevent cardiac arrest
Arrest (no-flow) phase (preserve)	• Minimize interval to BLS and ACLS (organized response) • Minimize interval to defibrillation, when indicated
Low-flow (CPR) phase (resuscitate)	• Push hard, push fast • Allow full chest recoil • Minimize interruptions in compressions • Avoid overventilation • Titrate CPR to optimize myocardial blood flow (coronary perfusion pressures and exhaled CO_2) • Consider adjuncts to improve vital organ perfusion during CPR • Consider ECMO if standard CPR/ALS not promptly successful
Postresuscitation phase: short-term	• Optimize cardiac output and cerebral perfusion • Treat arrhythmias, if indicated • Avoid hyperglycemia, hyperthermia, hyperventilation • Consider mild postresuscitation systemic hypothermia • Debrief to improve future responses to emergencies
Postresuscitation phase: longer term rehabilitation (regenerate)	• Early intervention with occupational and physical therapy • Bioengineering and technology interface • Possible future role for stem cell transplantation

Note: ALS, advanced life support; ACLS, advanced cardiac life support; BLS, basic life support; CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation.

ROSC. The same intense vasoconstriction during the postresuscitation phase may increase left ventricular afterload and worsen myocardial strain and dysfunction [35]. Current understanding of the physiology of cardiac arrest and recovery only enables the titration of blood pressure, global oxygen delivery and consumption, body temperature, inflammation, coagulation, and other physiologic parameters to attempt to optimize outcome. Future strategies will likely take advantage of emerging discoveries and knowledge of cellular inflammation, thrombosis, reperfusion, mediator cascades, cellular markers of injury and recovery, and transplantation technology.

Is Cardiopulmonary Resuscitation Effective for Children?

In Kouwenhoven and colleague's original report of successful resuscitation with closed chest cardiac massage [36], the initial patients were asphyxiated children in the operating room who received immediate effective resuscitation and attained excellent outcomes. When cardiac arrest is witnessed and of short duration, excellent outcomes *can* occur after various types of bystander CPR, including mouth-to-mouth rescue breathing alone, chest compressions alone, or standard chest compressions and mouth-to-mouth rescue breathing. Nevertheless, some reports question the effectiveness and advisability of prehospital pediatric CPR.

To further delineate these issues, prehospital pediatric asphyxial arrests were simulated in animal models. In the first study, asphyxia was induced by clamping of the tracheal tube of piglets until cardiac arrest occurred, defined by loss of aortic pulsation. The mean time until loss of aortic pulsations was 8.9 ± 0.4 min [37]. After loss of aortic pulsations, animals were randomized to simulated bystander CPR or no CPR until simulated EMS arrival 8 min later. After a complete cardiac arrest, 24-hr survival was clearly superior for the group who received both chest compressions and rescue breathing compared with either alone or no CPR. A similar study was performed with intervention at a slightly earlier point in the asphyxial process, when the pulse was *no longer palpable*, as defined by systolic pressure <50 mm Hg (i.e., after severe hypotension but before complete loss of aortic pulsation) [38]. After this injury without complete cardiac arrest, 24-hour survival was best when both chest compressions and rescue breathing were provided, but rescue breathing alone and chest compressions alone were individually better than no CPR at all [38]. Interestingly, most of the animals with 24-hour survival had ROSC before the simulated EMS arrival. Cardiopulmonary resuscitation was clearly not futile in these models of prehospital pediatric cardiac arrest; excellent CPR was remarkably effective when provided early enough.

Such laboratory studies put clinical reports in context. In a large, prospective study in Houston over 3.5 years, Sirbaugh and colleagues demonstrated that the outcomes from pediatric prehospital cardiac arrests were dismal: only 6 of the 300 children (2%) survived to hospital discharge, and only 1 of the 300 survived without significant neurologic deficits [23]. However, the diagnosis of cardiac arrest was determined by EMS providers when they arrived at the scene. As in most prehospital reports, children in cardiac arrest who attained ROSC after bystander CPR but before EMS arrival were excluded from analysis. Importantly, 41 children who had received bystander CPR were not in cardiac arrest at the time of EMS arrival; all 41 presumably had drowning-related cardiac arrests, and all survived with good neurologic outcomes [23]. Most exhibited evidence of significant hypoxic–ischemic injury when they arrived at the hospital, suggesting *real* cardiac arrest at the scene. In contrast, none of the other 24 children with drowning-related cardiac arrests who were still in cardiac arrest when the EMS personnel arrived survived with a good neurologic outcome.

Prospective evaluation of a decade-long, population-based study of pediatric drowning-related events in Houston demonstrated 421 children with drowning events in a population of ~2 million total and ~400,000 children (annual incidence of 10.0 per 100,000 children), and 234 required resuscitation [39]. One hundred ninety-three resuscitated children (82%) received bystander CPR, and 72% of these children were long-term survivors. Ninety-nine percent of the long-term survivors were neurologically intact. However, if the child was still apneic and pulseless when EMS personnel arrived, less than 5% were revived, and none of these subsequent survivors was ultimately neurologically intact [39]. These data and similar data from Hickey et al. [40] are consistent with the animal data, reported clinical experience, and in-hospital pediatric CPR data: CPR can be quite effective for asphyxial cardiac arrests, but timing of interventions is critically important.

In summary, animal and human data both indicate that CPR for children can be quite effective. In addition, these data support the idea that basic life support early is more important than advanced life support late. Prompt action by a citizen bystander in the prehospital setting or a provider in the in-hospital setting is generally more effective than late heroic efforts in our intensive care units.

Pediatric Ventricular Fibrillation

Ventricular fibrillation is an uncommon, but not rare, electrocardiographic (ECG) rhythm during out-of-hospital pediatric cardiac arrests. Two studies reported VF as the initial rhythm in 19%–24% of out-of-hospital pediatric cardiac arrests, but these studies excluded SIDS deaths. In studies that include SIDS victims, the frequency drops to the range of 6%–10% [41,42]. It is important to note that ECG rhythms are often not attained as promptly in children as in adults and that VF eventually converts into asystole over time. Therefore, the reported prevalence of VF is dependent on the aggressiveness and timing of monitoring and on the inclusion criteria for the report.

The incidence of VF varies by setting and age. In special circumstances, such as tricyclic antidepressant overdose, cardiomyopathy, postcardiac surgery, and prolonged QT syndromes, VF is a more likely rhythm during cardiac arrest. Commotio cordis, or mechanically initiated VF caused by relatively low-energy chest wall impact during a narrow window of repolarization (10–30 msec before the T-wave peak in swine models [43]), is reported, predominantly in children 4–16 years old. Out-of-hospital VF cardiac arrest is uncommon in infants but occurs more frequently in children and adolescents. The variance of VF by age was highlighted in a study documenting VF/VT in only 7.6% (10/131) of children in cardiac arrest 1–7 years old versus 27% of children 8–18 years old [42]. Although VF is often associated with underlying heart disease and generally considered the "immediate cause" of cardiac arrest, VF can occur secondary to asphyxia. In two studies of VF among asphyxiated piglets, the incidence of VF was 28% and 33% at some time during the cardiac arrest [37,38]. Asphyxia-associated VF is also well documented among pediatric near-drowning patients [39]. Furthermore, all VF is not the same, and VF that occurs as the initial rhythm during in-hospital cardiac arrests may be much different from VF occurring later in the arrest.

As noted above, in-hospital pediatric cardiac arrests are uncommon, but not rare, occurring in approximately 2% of PICU patients. Although the rhythms during most in-hospital cardiac arrests (in both children and adults) are asystole and pulseless electrical activity (PEA), in many arrests the rhythms are VF or pulseless VT. Among the first 1,005 pediatric in-hospital cardiac arrests in the American Heart Association's NRCPR (http://www.nrcpr.org/), 10% had an initial rhythm of VF/VT, an additional 15% had subsequent VF/VT (i.e., some time later during the resuscitation efforts), and another 2% had VF/VT but the timing of the arrhythmia was not clear. Therefore, 27% of children with in-hospital cardiac arrests had VF/VT, not an uncommon phenomenon [13]. Of note, survival to discharge was much more common among children with an initial shockable rhythm than among children with shockable rhythms occurring later during the resuscitation. Even in the setting of progressive respiratory failure and shock with an initial ECG of asystole or PEA, a substantial number of these children developed subsequent shockable VF/VT during CPR. Surprisingly, the subsequent VF/VT group had worse outcomes than children with asystole/PEA who never developed VF/VT during the resuscitation: 11% with subsequent VF/VT during resuscitation from asystole/PEA versus 27% with asystole/PEA alone. These data suggest that outcomes after *initial* VF/VT are *good*, but outcomes after *subsequent* VF/VT are substantially worse, even compared with asystole and/or PEA. Late shockable rhythms are presumed to be the result of progressive hypoxic–ischemic processes with expected poor outcomes. Traditionally, VF and VT have been considered *good* cardiac arrest rhythms, resulting in better outcomes than asystole and PEA. It is important to monitor the ECG early and repeatedly during resuscitation. Shockable rhythms of VF/VT can occur at some point in >25% of in-hospital pulseless cardiac arrests.

Termination of Ventricular Fibrillation: Defibrillation

Defibrillation (defined as termination of VF) is necessary for successful resuscitation from VF cardiac arrest. Note that termination of fibrillation can result in asystole, PEA, or a perfusing rhythm. The goal of defibrillation is return of an organized electrical rhythm with pulse. For example, prompt defibrillation provided soon after the induction of VF in a cardiac catheterization laboratory results in near-uniform successful defibrillation and survival. When automated external defibrillators (AEDs) are used within 3 min of witnessed VF, long-term survival can occur in more than 70% of victims [44]. In general, the mortality increases by 7%–10% per minute of delay to defibrillation [45,46]. Thus, provision of high-quality CPR can improve outcome and save lives. Because pediatric cardiac arrests are commonly caused by progressive asphyxia and/or shock, the initial treatment of choice is prompt CPR. Therefore, rhythm recognition in pediatrics tends to be relatively less emphasized than adult cardiac arrest situations. However, successful resuscitation from VF does require defibrillation such that the earlier that VF can be diagnosed, the more successfully it can be treated.

Determinants of Defibrillation (Termination of Ventricular Fibrillation)

Successful termination of VF (defibrillation) is achieved by attaining current flow adequate to depolarize a critical mass of myocardium. Current flow (amperes) is primarily determined by the shock energy (joules), which is selected by the operator, and the patient's transthoracic impedance (ohms). Animal studies in the 1970s with monophasic shock waveforms established that adequate electrical current flow through the myocardium led to successful defibrillation, whereas too much current flow resulted in postresuscitation myocardial damage and necrosis [47]. In addition, factors that affected transthoracic impedance were identified: paddle size, thoracic gas volume, electrode/paddle contact, and conducting paste [48]. Small paddle size increases resistance and thereby decreases current through the myocardium. On the other hand, paddles/pads larger than the heart result in current flow through extramyocardial pathways and thereby less current through the heart (consequently less flow for effective defibrillation). Poor electrode paddle contact and larger lung volumes (gas) result in greater impedance, whereas conducting paste and increased pressure at the paddle–skin contact decrease impedance. Transthoracic impedance could be decreased with multiple *stacked* shocks partly because of increased skin blood flow after electrical shocks. These studies established that current density (current flow through the myocardium) is the primary determinant of both effectiveness of the shock and myocardial damage [49].

Pediatric Defibrillation Dose

Early recommendations (1970s) for initial defibrillation doses as high as 200 J for all children were extrapolated from adult data. Despite clinical experience indicating that such doses were effective, providing these large energies to infants and children seemed potentially dangerous, with animal data demonstrating histopathologic myocardial damage at doses >10 J/kg [50,51] and suggesting 0.5–10 J/kg was adequate for defibrillation in a variety of species. Gutgesell and colleagues retrospectively evaluated the efficacy of a 2 J/kg pediatric defibrillation strategy [52]. Seventy-one transthoracic defibrillation attempts on 27 children were evaluated. These children were 3 days to 15 years old, and they weighed 2.1–50 kg. Fifty-seven of 71 shocks were within 10 J of the recommended 2 J/kg pediatric dose. Ninety-one percent (52/57) of these shocks were effective at terminating VF. The authors did not report any other outcome measures (e.g., successful termination of fibrillation to a perfusing rhythm, 24-hr survival, survival to discharge) [52]. Subsequent clinical usage suggests that the 2 J/kg dose is effective for short-duration in-hospital defibrillation [53], although this conclusion has not been rigorously evaluated.

As noted above, current density determines the effectiveness and harm of the shock. Moreover, differences in paddle size, defibrillation energy dose, and the individual's transthoracic impedance are the main determinants of current density. Therefore, Atkins and colleagues investigated the effects of paddle size, age, and weight on transthoracic impedance in children [54]. As expected, transthoracic impedance increased substantially with pediatric paddles. Based on those data, the American Heart Association recommends that *pediatric* or *small* paddles be used only for infants. More importantly, they established that the relationship between transthoracic impedance and weight is not linear [54]. The mean transthoracic impedance in their children was ~50 Ω with 83 cm^2 adult paddles and varied threefold among children. With *pediatric* or *small* pads (44 cm^2), the mean impedance was ~70 Ω in 3.8–36 kg children. The impedances of their infants were slightly lower than those of their older children, but the range of each was wide and the overlap substantial. Note that the mean transthoracic impedance in adults is typically ~60–80 Ω and also varies by more than

threefold. These data suggest that the adjustment of pediatric energy dose to weight (2–4 J/kg) requires further study.

Pediatric Defibrillation Doses for Prolonged Ventricular Fibrillation

Of the approximately 16,000 North American children with cardiac arrest each year, only 5%–20% present with an initial rhythm VF. There are few published data regarding pediatric defibrillation doses for prolonged VF. Therefore, the approach to pediatric prolonged VF is extrapolated from adult recommendations. For adults, the same defibrillation dose is recommended after brief duration or prolonged duration VF, even though the monophasic 200 J dose is often less effective at terminating prolonged VF (~60% termination of prolonged VF compared with >90% for short-duration VF). Defibrillation is typically with biphasic defibrillators, and the 150 or 200 J biphasic adult AED dosage is nearly 90% successful at terminating prolonged VF (much better than the ~60% effectiveness with 200 J monophasic defibrillation). The presently recommended pediatric VF dose of 2 J/kg by monophasic waveform is safe, but there are limited data on effectiveness for prolonged VF. A recently published animal study regarding defibrillation after 7 min of untreated VF in 4–24 kg piglets suggests that 2 J/kg may not be adequate [55]. Twenty-four piglets were shocked with 2 J/kg, followed by 4 J/kg. The pediatric dose of 2 J/kg monophasic shocks was uniformly unsuccessful at terminating fibrillation in all 24 piglets. This should not be overinterpreted; there could be interspecies differences in defibrillation thresholds. However, a small clinical study of pediatric defibrillation attempts also confirms that a 2 J/kg defibrillation dose is often inadequate. Eleven children received 14 pediatric dose shocks for VF in the Tucson emergency medical service over a 5-year period, using the same definition as Gutgesell did in his pediatric in-hospital (i.e., brief-duration) defibrillation study (2 J/kg ± 10 J). Only 7/14 shocks (50%) terminated out-of-hospital (prolonged) VF versus 52/57 shocks (91%) in their 27 in-hospital patients ($p < 0.01$). This small series suggests that further evaluation of shock dose for prolonged VF is important.

Standard weight-based dosing strategy for pediatric defibrillation is not easily implemented in AEDs. Manufacturers have developed alternatives that attenuate pediatric dose to 50–86 J biphasic. This dosage is safe and effective in piglets after either brief or prolonged VF. In addition, the 50 J/75 J/86 J shocks were more effective than a weight-based 2 J/kg dose at initial termination of fibrillation after prolonged VF [55]. Additional piglet studies modeling prolonged out-of-hospital pediatric VF (7 min of untreated VF), adult biphasic shocks of 200 J/300 J/360 J were compared with a *pediatric* biphasic AED dose of 50 J/75 J/86 J [56]. Pediatric dosing resulted in fewer elevations of cardiac troponin T levels, less postresuscitation myocardial dysfunction (i.e., lesser decreases of left ventricular ejection fraction 1–4 hr postresuscitation), and superior 24-hr survival with good neurologic outcome [56]. These data support the use of attenuating electrodes with adult AEDs for pediatric defibrillation. It is important to remember that no shock delivery for pediatric VF is 100% lethal. Therefore, adult defibrillation doses are preferable to no defibrillation dose. A single case report in the literature demonstrated that an adult AED dose could save the life of a 3-year-old child in VF [57]. That child was defibrillated with a biphasic shock of 150 J (9 J/kg). He survived without any apparent adverse effects. In particular, he had no elevations of serum creatine kinase or cardiac troponin I and normal postresuscitation ventricular function on ECG.

Pediatric Automated External Defibrillators

Ventricular fibrillation is prolonged in nearly all children with out-of-hospital VF by the time emergency medical service personnel and defibrillators arrive. Recently, AEDs were recommended for children <8 years old [58]. Two issues had to be considered before such recommendations: (1) the safety and efficacy of the AED diagnostic rhythm analysis program in children and (2) the safety and efficacy of the AED shock dosage. An important concern was that babies and small children with sinus tachycardia or supraventricular tachycardia can have very high heart rates that might be misinterpreted as *shockable* by AEDs with diagnostic programs developed for adult arrhythmias. Fortunately, published studies regarding the rhythm analysis programs from several manufacturers have established that they are quite sensitive and specific in detecting the shockable rhythm of VF [53,59,60]. Both algorithms were less sensitive at detecting the very uncommon shockable rhythm of VT, but were quite specific (i.e., the algorithm did not misinterpret other rhythms as VT and therefore did not recommend shocking a *nonshockable* rhythm). Ideally the device should demonstrate high specificity for pediatric shockable rhythms, that is, the device will not recommend a shock for *nonshockable rhythms*. Currently the evidence is insufficient to support a recommendation for or against the use of AEDs in children <1 year of age.

Interventions During the Low-Flow Phase: Cardiopulmonary Resuscitation

Airway and Breathing

One of the most common precipitating events for cardiac arrests in children is respiratory insufficiency. Adequate oxygen delivery to meet metabolic demand and removal of carbon dioxide is the goal of initial assisted ventilation. Effective bag-mask ventilation remains the cornerstone of providing effective emergency ventilation. Effective ventilation does not necessarily require an endotracheal tube. In one randomized, controlled study of children with out-of-hospital respiratory arrest, children who were treated with bag-mask ventilation did as well as children treated with prehospital endotracheal intubation [61]. Emergency airway techniques such as transtracheal jet ventilation and emergency cricothyroidotomy are rarely, if ever, required during CPR. During CPR, cardiac output and pulmonary blood flow are approximately 10%–25% of that during normal sinus rhythm. Consequently, much less ventilation is necessary for adequate gas exchange from the blood traversing the pulmonary circulation during CPR. Animal and adult data indicate that overventilation during CPR is common and can substantially compromise venous return and cardiac output [32]. Most concerning, these adverse hemodynamic effects during CPR combined with the interruptions in chest compressions typically necessary to provide airway management and rescue breathing can contribute to worse survival outcomes.

Although *airway* and *breathing* are prioritized in the ABC assessment approach, special circumstances may impact that priority order. In animal models of sudden VF cardiac arrest, acceptable PaO_2 and $PaCO_2$ persist for 4 to 8 min during chest compressions without rescue breathing [62]. Moreover, many animal studies indicate that outcomes from sudden short-duration VF cardiac arrests are at least as good with chest compressions alone as with chest compressions plus rescue breathing. In addition, several retrospec-

tive studies of witnessed VF cardiac arrest in adults also suggest that outcomes are similar after bystander-initiated CPR with either chest compressions alone or chest compressions plus rescue breathing. A randomized, controlled study of dispatcher-assisted bystander CPR in adults found a trend toward improved survival in the patients who received chest compressions alone compared with those who received dispatcher-instructed ventilation and chest compressions [63,64]. In contrast, animal studies of asphyxia-precipitated cardiac arrests have established that rescue breathing is a critical component of successful CPR.

Because adequate oxygenation and ventilation are important for survival from any cardiac arrest, why is rescue breathing not initially necessary for VF yet quite important in asphyxia? Immediately after an acute fibrillation-induced cardiac arrest, aortic oxygen and carbon dioxide concentrations do not vary from the prearrest state, because there is no blood flow and aortic oxygen consumption is minimal. Therefore, when chest compressions are initiated, the blood flowing from the aorta to the coronary and cerebral circulations provides adequate oxygenation at an acceptable pH. At that time, myocardial oxygen delivery is limited more by blood flow than by oxygen content [65]. Adequate oxygenation and ventilation can continue without rescue breathing, because the lungs serve as a reservoir for oxygen during the low-flow state of CPR. In addition, ventilation can occur because of chest compression-induced gas exchange and spontaneous gasping during CPR in victims of sudden cardiac arrest. Therefore, arterial oxygenation and pH can often be adequate with chest compressions alone for VF arrests.

It remains important to note that, for the infant or child, forgoing ventilation may not be appropriate, because respiratory arrest and asphyxia generally precede pediatric cardiac arrest. During asphyxia, blood continues to flow to tissues; therefore, arterial and venous oxygen saturations decrease while carbon dioxide and lactate increase. In addition, continued pulmonary blood flow before the cardiac arrest depletes the pulmonary oxygen reservoir. Therefore, asphyxia results in significant arterial hypoxemia and acidemia before resuscitation in contrast to VF. In this circumstance, rescue breathing can be life saving.

Circulation

Basic life support with continuous effective chest compressions is generally the best way to provide circulation during cardiac arrest. Basic life support is often provided poorly or not provided at all. The most critical elements are to *push hard* and *push fast* [30]. Because there is no flow without chest compressions, it is important to minimize interruptions in chest compressions. To allow good venous return in the decompression phase of external cardiac massage, it is important to allow full chest recoil and to avoid overventilation. The latter can prevent venous return because of increased intrathoracic pressure.

The use of closed-chest cardiac massage to provide adequate circulation during cardiac arrest was initially demonstrated in small dogs with compliant chest walls. Based on reasonable extrapolation, these investigators felt that closed-chest cardiac massage would be effective with children but might not be with adults. Therefore, the first patients successfully treated with closed-chest cardiac massage were children [36,66]. The presumed mechanism of blood flow was direct compression of the heart between the sternum and the spine in these children with compliant chest walls. Later investigations indicated that blood can also be circulated during CPR by the thoracic pump mechanism [67,68]. That is, chest compression-induced increases in intrathoracic pressure can generate a gradient for blood to flow from the pulmonary vasculature, through the heart, and into the peripheral circulation (e.g., thoracic pump mechanism). Regardless of mechanism, cardiac output during CPR seems to be greater in children (and immature animals) with compliant chest walls than in adults with less compliant chest walls.

Circumferential Versus Focal Sternal Compressions

In adults and animal models of cardiac arrest, circumferential (Vest) CPR provides better CPR hemodynamics than point compressions. In smaller infants, it is often possible to encircle the chest with both hands and depress the sternum with the thumbs while compressing the thorax circumferentially. In an infant model of CPR, this "two-thumb" method of compression resulted in higher systolic and diastolic blood pressures and a higher pulse pressure than did traditional two-finger compression of the sternum.

Duty Cycle

Duty cycle is the ratio of time of compression phase to the entire compression–relaxation cycle. In a model of human adult cardiac arrest, cardiac output and coronary blood flow are optimized when chest compressions last for 30% of the total cycle time [69]. As the duration of CPR increases, the optimal duty cycle may increase to 50%. In a juvenile swine model, a relaxation period of 250–300 msec (a duty cycle of 40%–50% if 120 compressions are delivered per minute) correlates with improved cerebral perfusion pressure when compared with shorter duty cycles of 30%.

Open-Chest Cardiopulmonary Resuscitation

Excellent standard closed-chest CPR generates approximately 10%–25% of baseline myocardial blood flow and a cerebral blood flow that is approximately 50% of normal. By contrast, open-chest CPR can generate a cerebral blood flow that approaches normal. Although open-chest massage improves coronary perfusion pressure and increases the chance of successful defibrillation in animals and humans, surgical thoracotomy is impractical in many situations. A retrospective review of 27 cases of CPR following pediatric blunt trauma (15 with open-chest CPR and 12 with closed-chest CPR) demonstrated that open-chest CPR increased hospital cost without altering rates of ROSC or survival to discharge [70]. However, survival in both groups was 0%, indicating that the population may have been too severely injured or too late in the process to benefit from this aggressive therapy. Open-chest CPR is often provided to children after open-heart cardiac surgery and sternotomy. Earlier institution of open-chest CPR may warrant reconsideration in selected special resuscitation circumstances.

Ratio of Compressions to Ventilation

Compression/ventilation ratios and tidal volumes recommended during CPR are based on rational conjecture and educational retention theory. Ideal compression/ventilation ratios for pediatric patients are unknown. Recent physiologic estimates suggest the amount of ventilation needed during CPR is much less than the amount needed during a normal perfusing rhythm because the cardiac output during CPR is only 10%–25% of that during normal sinus rhythm. The benefits of positive pressure ventilation

(increased arterial content of oxygen and carbon dioxide elimination) must be balanced against the adverse consequence of impeding circulation.

Maximizing systemic oxygen delivery during single-rescuer CPR requires a tradeoff between time spent doing chest compressions and time spent doing mouth-to-mouth ventilations. Theoretically, neither compression-only nor ventilation-only CPR can sustain systemic oxygen delivery. The best ratio depends on many factors, including the compression rate, the tidal volume, the blood flow generated by compressions, and the time that compressions are interrupted to perform ventilations [71]. A chest compression to ventilation ratio of 15:2 delivered the same minute ventilation as CPR with a chest compression to ventilation ratio of 5:1 in a mannequin model of pediatric CPR, but the number of chest compressions delivered was 48% higher with the 15:2 ratio [72].

In adults, mathematical models of oxygen delivery during CPR performed with variable ratios of health care provider chest compressions to ventilations suggest the optimal compression to ventilation ratio is approximately 30:2 and for lay rescuers closer to 50:2. Mathematical models of compression/ventilation ratios suggest that matching of the amount of ventilation to the amount of reduced pulmonary blood flow during closed-chest cardiac compressions should favor very high compression/ventilation ratios. Babbs and Kern chose to demonstrate the effect of compression/ventilation ratio on oxygen delivery to peripheral tissues [73]. Maximizing oxygen delivery to peripheral tissues during single-rescuer CPR requires a tradeoff between the time required to compress the chest and time required to provide rescue breathing. Ignoring the amount of ventilation provided by chest compressions alone, neither compression-only nor ventilation-only CPR can sustain oxygen delivery to the periphery for prolonged periods of CPR.

The best ratio depends upon many factors, including the compression rate, the tidal volume, the blood flow generated by compressions, and the time that compressions are interrupted to perform ventilations. These factors can be related in a mathematical formula based upon physiology. These variables change as a function of the size of the patient. Such considerations may help refine the amount of ventilation recommended for both adults and children. The ratio of chest compressions to ventilations during *no-flow* and *low-flow* phases of cardiopulmonary–cerebral resuscitation remains an area of high interest, controversy, and future research. These formulas adjusted to the known physiologic variables in children have suggested the potential to simplify the compression/ventilation ratio to 15 chest compressions: 2 ventilations in children.

Intraosseous Vascular Access

Intraosseous vascular access provides access to a noncollapsible marrow venous plexus, which serves as a rapid, safe, and reliable route for administration of drugs, crystalloids, colloids, and blood during resuscitation. Intraosseous vascular access often can be achieved in 30 to 60 sec. Although a styleted, specially designed intraosseous bone marrow needle is preferred to prevent obstruction of the needle with cortical bone, butterfly needles and standard hypodermic needles have been successfully used. The intraosseous needle is typically inserted into the anterior tibial bone marrow; alternative sites include the distal femur, medial malleolus or the anterior superior iliac spine, and the distal tibia. In adult and older children, the medial malleolus, distal radius, and distal ulna are optional locations.

Resuscitation drugs, fluids, continuous catecholamine infusions, and blood products can be safely administered by the intraosseous route. Onset of action and drug levels following intraosseous infusion during CPR are comparable with those achieved following vascular administration, including central venous administration. Intraosseous vascular access may also be used to obtain blood specimens for chemistry, blood gas analysis, and type and crossmatch, although administration of sodium bicarbonate through the intraosseous cannula eliminates the close correlation with mixed venous blood gases.

Complications have been reported in less than 1% of patients following intraosseous infusion [74]. Complications include tibial fracture, lower extremity compartment syndrome, severe extravasation of drugs, and osteomyelitis. Most of these complications may be avoided by careful technique. Although microscopic pulmonary fat and bone marrow emboli have been demonstrated in animal models, they have never been reported clinically and appear to occur just as frequently during cardiac arrest without intraosseous drug administration. Animal data and one human follow-up study indicate that local effects of intraosseous infusion on the bone marrow and bone growth are minimal.

Medication Use During Cardiac Arrest

Although animal studies indicate that epinephrine can improve initial resuscitation success after both asphyxial and VF cardiac arrests, no single medication has been shown to improve survival outcome from pediatric cardiac arrest.

Tracheal Drug Administration

Intraosseous vascular access has largely replaced the need for tracheal drug administration. Important drugs could be administered via the tracheal tube before vascular access was achieved. In particular, lidocaine, atropine, naloxone, and epinephrine were commonly administered via the tracheal route. Note that sodium bicarbonate and calcium may be very irritating to the airways and lung parenchyma, so they are not recommended for tracheal administration. Absorption of drugs into the circulation after tracheal administration depends on dispersion over the respiratory mucosa, pulmonary blood flow, and the matching of the ventilation (drug dispersal) to perfusion. The small volumes of drug that remain as droplets in the tracheal tube are obviously not effective. Inadequate chest compressions resulting in poor pulmonary blood flow will also limit absorption of the drug and prevent its delivery to the heart and systemic circulation. Preexisting pathophysiologic conditions such as pulmonary edema, pneumonitis, and airway disease also affect the pharmacokinetics of tracheally administered drugs. Another confounding factor is that the vasoconstrictive effects of epinephrine may limit local pulmonary blood flow, thereby diminishing drug uptake and delivery. It is therefore not surprising that drug absorption varies greatly and that optimal drug doses have not been determined. Animal studies reveal a wide variability in plasma epinephrine levels and physiologic effects after endotracheal administration. On average, 10 times as much tracheal epinephrine is needed to attain peak plasma levels comparable to intravenous administration. Moreover, a prolonged depot effect typically occurs after tracheal epinephrine administration, which can lead to postresuscitation hypertension, tachycardia, and ventricular arrhythmias.

Vasopressors

During CPR, epinephrine's α-adrenergic effect on vascular tone is most important. The α-adrenergic action increases systemic vascular resistance, thereby increasing diastolic blood pressure, which in turn increases coronary perfusion pressure and blood flow and increases the likelihood of ROSC. Epinephrine also increases cerebral blood flow during CPR because peripheral vasoconstriction directs a greater proportion of flow to the cerebral circulation. The β-adrenergic effect increases myocardial contractility and heart rate and relaxes smooth muscle in the skeletal muscle vascular bed and bronchi, although this effect is of less importance. Epinephrine also increases the vigor and intensity of VF, increasing the likelihood of successful defibrillation.

High-dose epinephrine (0.05–0.2 mg/kg) improves myocardial and cerebral blood flow during CPR more than standard-dose epinephrine (0.01–0.02 mg/kg) and may increase the incidence of initial ROSC [75,76]. Administration of high-dose epinephrine, however, can worsen a patient's postresuscitation hemodynamic condition with increased myocardial oxygen demand, ventricular ectopy, hypertension, and myocardial necrosis. Studies indicate that use of high-dose epinephrine in adults or children does not improve survival and may be associated with a worse neurologic outcome [76,77].

A randomized, controlled trial of rescue high-dose epinephrine versus standard-dose epinephrine following failed initial standard-dose epinephrine for pediatric in-hospital cardiac arrest demonstrated a worse 24-hr survival rate in the high-dose epinephrine group (1/27 vs. 6/23, $p < 0.05$) [3]. In particular, high-dose epinephrine seemed to worsen the outcome of patients with asphyxia-precipitated cardiac arrest. High-dose epinephrine cannot be recommended routinely for initial therapy or rescue therapy.

Wide variability in catecholamine pharmacokinetics and pharmacodynamics dictate individual titration. A life-saving dose during CPR for one patient may be life threatening to another. High-dose epinephrine should be considered as an alternative to standard-dose epinephrine in special circumstances of refractory pediatric cardiac arrest (e.g., patient on high-dose epinephrine infusion before cardiac arrest) and/or when continuous direct arterial blood pressure monitoring allows titration of the epinephrine dosage to diastolic (decompression phase) arterial pressure during CPR. Nevertheless, high-dose epinephrine has not been demonstrated to improve outcome and should only be used with caution.

Vasopressin is a long-acting endogenous hormone that acts at specific receptors to mediate systemic vasoconstriction (V_1 receptor) and reabsorption of water in the renal tubule (V_2 receptor). In experimental models of cardiac arrest, vasopressin increases blood flow to the heart and brain and improves long-term survival compared with epinephrine. Vasopressin may decrease splanchnic blood flow during and following CPR. In randomized controlled trials of in-hospital and out-of-hospital arrests in adults, vasopressin had comparable efficacy to epinephrine [78]. Vasopressin did not improve outcome compared with epinephrine.

In a pediatric porcine model of prolonged VF, the use of vasopressin and epinephrine in combination resulted in higher left ventricular blood flow than either pressor alone, and both vasopressin alone and vasopressin plus epinephrine resulted in superior cerebral blood flow than epinephrine alone [79–82]. By contrast, in a pediatric porcine model of *asphyxial* cardiac arrest, ROSC was more likely in piglets treated with epinephrine than in those treated with vasopressin [83]. A case series of four children who received vasopressin during six prolonged cardiac arrest events suggests that the use of bolus vasopressin may result in ROSC when standard medications have failed [84]. Vasopressin has also been reported to be useful in low cardiac output states associated with sepsis syndrome and organ recovery in children. While vasopressin will not likely replace epinephrine as a first-line agent in pediatric cardiac arrest, there are preliminary data to suggest that its use in conjunction with epinephrine in pediatric cardiac arrest deserves further investigation [85].

Calcium

For in-hospital pediatric cardiac arrests, hypocalcemia is not uncommon. Although calcium administration is only recommended during cardiac arrest for hypocalcemia, hyperkalemia, hypermagnesemia, and calcium channel blocker overdose, it is commonly used for in-hospital pediatric cardiac arrests, especially those occurring after cardiac surgery. The administration of calcium has not been demonstrated to improve outcome in cardiac arrest. Animal studies suggest that calcium administration may worsen reperfusion injury [86].

Buffer Solutions

Cardiac arrest results in lactic acidosis from inadequate organ blood flow and poor oxygenation. Acidosis depresses myocardial function, reduces systemic vascular resistance, and inhibits defibrillation. Nevertheless, the routine use of sodium bicarbonate for a child in cardiac arrest is not recommended. Clinical trials involving critically ill adults with severe metabolic acidosis did not demonstrate a beneficial effect of sodium bicarbonate. However, the presence of acidosis may depress the action of catecholamines, so the use of sodium bicarbonate seems rational in an acidemic child who is refractory to catecholamine administration. The administration of sodium bicarbonate is more clearly indicated for the patient with a tricyclic antidepressant overdose, hyperkalemia, hypermagnesemia, or sodium channel blocker poisoning.

The buffering action of bicarbonate occurs when a hydrogen cation and a bicarbonate anion combine to form carbon dioxide and water. If carbon dioxide is not effectively cleared through ventilation, its build-up will counterbalance the buffering effect of bicarbonate. Other side effects with sodium bicarbonate include hypernatremia, hyperosmolarity, and metabolic alkalosis. Tris-hydroxymethyl aminomethane (THAM) is a noncarbon dioxide generating buffer that can be used during cardiac arrest. Note that excessive alkalosis decreases calcium and potassium concentration and shifts the oxyhemoglobin dissociation curve to the left.

Antiarrhythmic Medications: Lidocaine and Amiodarone

Administration of antiarrhythmic medications should not delay administration of a shock for a patient with VF. However, after unsuccessful attempts at electrical defibrillation, medications to increase the effectiveness of defibrillation should be considered. For both pediatric and adult patients, the first administered medication for VF is epinephrine. If epinephrine with or without vasopressin and a subsequent repeat attempt to defibrillate are unsuccessful, the antiarrhythmic agents amiodarone or lidocaine should be considered.

Lidocaine has been recommended traditionally for shock-resistant VF in adults and children. However, the only antiarrhythmic agent that has been prospectively determined to improve survival to hospital admission in the setting of shock-resistant VF when compared to placebo is amiodarone. Furthermore, patients who received amiodarone for shock-resistant out-of-hospital VF had a higher rate of survival to hospital admission than patients who received lidocaine alone [87,88]. Neither of these randomized controlled trials included children. Although there are no published comparisons of antiarrhythmic medications for pediatric refractory VF, extrapolation of the adult studies has led to the recommendation of amiodarone as the preferred antiarrhythmic agent for children.

Postresuscitation Interventions

Temperature Management

Mild induced hypothermia is the most celebrated goal-directed postresuscitation therapy for adults. Two seminal articles established that induced hypothermia (32°–34°C) could improve outcome for comatose adults after resuscitation from VF cardiac arrest [33,34]. In both randomized controlled trials, the inclusion criteria were patients older than 18 years who were persistently comatose after successful resuscitation from nontraumatic VF. The multicenter European study had a goal of 32°–34°C for the first 24 hr postarrest. The mean time until attainment of this temperature goal was 8 hr. Six-month survival with good neurologic outcome was superior in the hypothermic group (75/136 vs. 54/137 with RR of 1.40 [CI, 1.08–1.81]) [34]. Similarly, death at 6 months postevent occurred less often in the hypothermic group (56/137 vs. 76/138; RR of 0.74 [CI, 0.58–0.95]) [34]. Bernard et al. reported good outcomes in 21/43 (49%) of the hypothermic group versus 9/34 (26%) of the control group, (p = 0.046, OR 5.25 [CI, 1.47–18.76]) [33]. Importantly, hypotension occurred in over half of the patients in both groups and was aggressively treated with vasoactive infusion in the European study. Similarly, more than half of the patients in the Bernard et al. study received epinephrine infusions during the first 24 hours postresuscitation [33].

Interpretation and extrapolation of these studies to children is difficult. Fever following cardiac arrest is associated with poor neurologic outcome, and hyperthermia following cardiac arrest is common in children. It is reasonable to believe that mild induced systemic hypothermia may benefit children resuscitated from cardiac arrest. However, benefit from this treatment has not been rigorously studied and reported in children or in any patients with non-VF arrests. At a minimum, it is advisable to avoid even mild hyperthermia in children following CPR. Scheduled administration of antipyretic medications *and* use of external cooling devices are often necessary to avoid hyperthermia in this population.

Postresuscitation Myocardial Support

Postarrest myocardial stunning occurs commonly after successful resuscitation in animals, adults, and children. In addition, most adults who survive to hospital admission after an out-of-hospital cardiac arrest die in the postresuscitation phase, many due to progressive myocardial dysfunction. Animal studies demonstrate that postarrest myocardial stunning is characterized by a global biventricular systolic and diastolic dysfunction, and typically resolves after 1 or 2 days [89]. Postarrest myocardial stunning is pathophysiologically similar to sepsis-related myocardial dysfunction and postcardiopulmonary bypass myocardial dysfunction, including increases in inflammatory mediator and nitric oxide production. Postarrest myocardial stunning is worse after a more prolonged untreated cardiac arrest, after more prolonged CPR, after defibrillation with higher energy shocks, and after a greater number of shocks [90].

Optimal treatment of postarrest myocardial dysfunction has not been established. As noted earlier, this myocardial dysfunction has been treated with various continuous inotropic/vasoactive agents, including dopamine, dobutamine, and epinephrine, in both children and adults. In addition, milrinone improves the hemodynamic status of children with postcardiopulmonary bypass myocardial dysfunction and septic shock. Finally, the new inotropic agent levosimenden has also been effective in animal models of postresuscitation myocardial dysfunction. Although prospective controlled trials in animals have demonstrated that the myocardial dysfunction can be effectively treated with vasoactive agents, there are no data demonstrating improvements in outcome. Nevertheless, because myocardial dysfunction is common and can lead to secondary ischemic injuries to other organ systems or even cardiovascular collapse, treatment with vasoactive medications is a rational therapeutic choice that may improve outcome. The hemodynamic benefits in animal studies of postarrest myocardial dysfunction, pediatric studies of postcardiopulmonary bypass myocardial dysfunction, and pediatric sepsis-related myocardial dysfunction support the use of inotropic/vasoactive agents in this setting. In addition, adult studies document the common occurrence of postarrest hypotension and/or poor myocardial function "requiring" inotropic/vasoactive agents. In summary, because treatment of postarrest myocardial dysfunction with inotropic/vasoactive infusions can improve the patient's hemodynamic status, such treatment should be routinely considered and titrated to effect. Unfortunately, evidence-based therapeutic targets for goal-directed therapy are ill defined.

Blood Pressure Management

Laurent and colleagues demonstrated that 55% of adults surviving out-of-hospital cardiac arrests required in-hospital vasoactive infusions for hypotension unresponsive to volume boluses [91]. Compared with healthy volunteers, adults resuscitated from cardiac arrest have impaired autoregulation of cerebral blood flow. Hence, they may not maintain cerebral perfusion pressure in the face of systemic hypotension and likewise may not be able to protect the brain from acutely increased blood flow in the face of systemic hypertension. It is rational to presume that blood pressure variability should be minimized as much as possible following resuscitation from cardiac arrest.

A brief period of hypertension following resuscitation from cardiac arrest may diminish the no-reflow phenomenon. In animal models, brief induced hypertension following resuscitation results in improved neurologic outcome compared with normotension [92]. As retrospective human studies suggest that postresuscitative hypertension was associated with a better neurologic outcome after controlling for age, gender, duration of cardiac arrest, duration of CPR, and preexisting diseases, it seems reasonable to aggressively treat and prevent hypotension [93].

Glucose Control

Hyperglycemia following adult cardiac arrest is associated with worse neurologic outcome after controlling for duration of arrest and presence of cardiogenic shock [94–96]. In an animal model of asphyxial cardiac arrest, administration of insulin and glucose, but not administration of glucose alone, improved neurologic outcome compared with administration of normal saline [97]. Data for evidence-based titration of specific endpoints are not available.

Extracorporeal Membrane Oxygenation–Cardiopulmonary Resuscitation

Perhaps the ultimate technology to control postresuscitation temperature and hemodynamic parameters is extracorporeal membrane oxygenation (ECMO). In addition, the concomitant administration of heparin may optimize microcirculatory flow. The use of venoarterial ECMO to reestablish circulation and provide controlled reperfusion following cardiac arrest has been published [98–101], but prospective, controlled studies are lacking. Nevertheless, these series have reported extraordinary results with the use of ECMO as a rescue therapy for pediatric cardiac arrests, especially from potentially reversible acute postoperative myocardial dysfunction or arrhythmias. In one study, 11 children who suffered cardiac arrest in the pediatric intensive care unit after cardiac surgery were placed on ECMO during CPR after 20–110 min of CPR [102]. Prolonged CPR was continued until ECMO cannulas, circuits, and personnel were available. Six of these 11 children were long-term survivors without apparent neurologic sequelae [102]. Increasingly improved survival rates have been reported for pediatric cardiac patients provided with mechanical cardiopulmonary support within 20 min of the initiation of CPR. Despite these promising results, CPR and ECMO are not curative treatments; rather, they are simply cardiopulmonary supportive measures that may allow tissue perfusion and viability until recovery from the precipitating disease process can occur. Most remarkably, Morris et al. reported 66 children who over 7 years were placed on ECMO during CPR at Children's Hospital of Philadelphia [101]. The median duration of CPR before establishment of ECMO was 50 min, and 35% (23/66) of these children survived to hospital discharge. It is important to emphasize that these children had brief periods of "no flow," excellent CPR during the "low-flow" period, and a well-controlled postresuscitation phase. Potential advantages of ECMO come from its ability to maintain tight control of physiologic parameters after resuscitation. Parameters including blood flow rates, oxygenation, ventilation, anticoagulation, and body temperature can all be manipulated precisely through the ECMO circuit. As we learn more about the processes of secondary injury following cardiac arrest, ECMO might enable controlled perfusion and temperature management to minimize reperfusion injury and maximize cell recovery.

Neuropsychological Issues

Information about neurologic outcomes and predictors of neurologic outcome after both adult and pediatric cardiac arrests is limited. Barriers to assessment of neurologic outcomes of children after cardiac arrests include the constantly changing developmental context that occurs with brain maturation. Prediction or prognosis for future neuropsychological status is a complex task, particularly after an acute neurologic insult. There is little information about the predictive value of clinical neurologic examinations, neurophysiologic diagnostic studies (e.g., electroencephalographic [EEG] or somatosensory evoked potentials) [103,104], biomarkers [105], or imaging (computed tomography, magnetic resonance imaging [MRI], or positron emission tomography) on eventual outcome following cardiac arrest or other global hypoxic–ischemic insults in children. Computed tomography scans are not sensitive in detecting early neurologic injury. The value of MRI studies following pediatric cardiac arrest is not yet clear; however, MRI with diffusion weighting should provide valuable information about hypoxic–ischemic injury in the subacute and recovery phases.

Emerging data suggest that burst-suppression pattern on postarrest EEG is sensitive and specific for poor neurologic outcome [106,107]. Studies have shown that somatosensory evoked potential (SSEP) can be highly sensitive and specific in pediatric patients after cardiac arrest [108,109]. However, SSEP is not standardized in the pediatric population and is difficult to interpret. Many children who suffer a cardiac arrest have substantial preexisting neurologic problems. For example, 17% of the children with in-hospital cardiac arrests from the NRCPR were neurologically abnormal before the arrest. Thus, comparison with prearrest neurologic function of a child is difficult and adds another dimension/barrier to the assessment and prediction of postarrest neurologic status.

Biomarkers are emerging tools to predict neurologic outcome. In an adult study, serum level of neuron-specific enolase (NSE) and S-100b protein showed prognostic value. Elevated NSE and S-100b were highly sensitive and specific for poor neurologic outcome (death or persisting unconsciousness) [110]. The validation of these biomarkers in pediatric postarrest patients requires further study.

Most pediatric cardiac arrest outcome studies have not included neurologic outcomes. Investigations that include neurologic outcomes have generally used the Pediatric Cerebral Performance Category, a gross outcome scale. Many neuropsychological tests can detect more subtle, clinically important neuropsychological sequelae from neurologic insults. Neuropsychological outcomes are important issues for future pediatric cardiac arrest outcome studies.

Conclusion

Despite evidence-based guidelines, extensive provider training, and provider credentialing in resuscitation medicine, the quality of CPR and resuscitation science lacks high quality. Tremendous impact of simple, immediate actions such as "push hard, push fast, minimize interruptions, allow full chest recoil and do not overventilate" can markedly improve outcomes. Directive and corrective real-time feedback, combined with team dynamic training and debriefing, can substantially improve self-efficacy and operational performance.

Outcomes from pediatric cardiac arrest and CPR appear to be improving. Evolving understanding of the pathophysiology of events and titration of the interventions to the timing, etiology, duration, and intensity of the cardiac arrest event can improve resuscitation outcomes. Exciting discoveries in basic and applied science are on the immediate horizon for study in specific

populations of cardiac arrest victims. By strategically focusing therapies to specific phases of cardiac arrest and resuscitation and to evolving pathophysiology, there is great promise that critical care interventions will lead the way to more successful cardiopulmonary and cerebral resuscitation in children. Treatment of sudden death in children in the future requires more evidence-based and less anecdotal interventions. Timing of therapeutic interventions to prevent arrest and to protect, preserve, and promote restoration of intact neurologic survival is of the highest priority.

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