PITTSBURGH CRITICAL CARE MEDICINE

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Pediatric Intensive Care

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Series Preface

No place in the world is more closely identified with critical care medicine than Pittsburgh. In the late 1960s, Peter Safar and Ake Grenvik pioneered the science and practice of critical care not just in Pittsburgh, but around the world. Their multidisciplinary team approach became the standard for how intensive care unit care is delivered in Pittsburgh to this day. The Pittsburgh Critical Care Medicine series honors this tradition. Edited and authored largely by University of Pittsburgh faculty, the content reflects best practice in critical care medicine. The Pittsburgh model has been adopted by many programs worldwide, and local leaders are recognized as world leaders. It is our hope that, through this series of concise handbooks, a small part of this tradition can be passed on to the many practitioners of critical care the world over.

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Chapter 1

Resuscitation and Stabilization

Vinay Nadkarni, Robert M. Sutton, and Robert A. Berg

Approximately 16,000 children (8–20/100,000 children/y) have a cardiopulmonary arrest event in North America each year: half out-of-hospital, with 3% to 12% survival to hospital discharge, and half in-hospital, with 27% to 48% survival to hospital discharge (see Box 1.1). Approximately 2% to 6% of all children admitted to pediatric intensive care units and 4% to 6% of children admitted to cardiac intensive care units experience a cardiac arrest. With implementation of early warning scores and rapid response teams, more than 95% of pediatric cardiac arrests occur in intensive care areas, not in wards. With advances in early detection and response, survival from pediatric cardiac arrest has improved substantially during the past 25 years. About 75% of cardiac arrest survivors have good neurological outcome, and more than 90% who survive to discharge are alive 1 year later.

Key Messages

- The four phases of cardiac arrest and cardiopulmonary resuscitation (CPR) are (1) prearrest, (2) no flow (untreated cardiac arrest), (3) low flow (CPR), (4) postresuscitation (see Figure 1.1).
- The most common precipitating event for cardiac arrests in children is respiratory failure, progressing to bradycardia and then pulseless electrical activity, or asystole; therefore, support of oxygenation and ventilation is a high priority before loss of pulses.
- The most treatable form of sudden cardiac arrest is witnessed ventricular fibrillation, with prompt recognition, CPR, and defibrillation shock.
- High-quality CPR requires you to
  1. Push hard, push fast (approximately 100−120 times per minute)
  2. Allow full chest recoil between compressions
  3. Minimize interruptions
  4. Avoid overventilation (rescue breaths at approximately 10 times per minute)
- Good-quality CPR is tiring. Switch chest compressors approximately every 2 minutes.

Box 1.1 Overview of Pediatric Cardiac Arrest

Out-of-Hospital Pediatric Cardiac Arrest

Respiratory etiology

Poor outcome (3%–12% survival to discharge, with ~66% good neurological outcome)

Rare witnessed, monitored, or shockable initial rhythms

In-Hospital Pediatric Cardiac Arrest

Combined respiratory and cardiac etiology

Seventy percent survive event, 27% to 48% survive to discharge (~75% good neurological outcome)

Commonly witnessed, monitored, and shockable (10%–15% initial rhythm)

- Rapid vascular access can be obtained with an intraosseous (IO) needle to deliver epinephrine at a 0.01-mg/kg/dose.
- Feedback on depth of compressions, end-tidal carbon dioxide target >20 mm Hg, and diastolic blood pressure >25 mm Hg can be used to guide quality of chest compressions and vasopressor administration during CPR.
- Attention to meticulous postresuscitation care can improve survival outcomes—specifically, (1) avoid hypotension, (2) manage targeted temperature to avoid hyperthermia, (3) normalize ventilation, (4) titrate oxygen to avoid hyperoxia or hypoxia (usual target 94%–99% oxygen saturation), (5) identify and treat seizures, and (6) avoid hypoglycemia and hyperglycemia.
- Consider family presence during resuscitation with appropriate dedicated support/guidance provided to family members.

Prearrest Phase

The prearrest phase focuses on early recognition and prevention of progression of relevant preexisting conditions (e.g., sepsis, pulmonary hypertension, shock, electrolyte abnormality, severe hypothermia, abdominal competition with breathing) to become precipitating events (e.g., respiratory failure, hypotensive shock, pulmonary hypertension with hypoxemia). Children who experience an in-hospital cardiac arrest often have changes in their physiological status in the hours leading up to their arrest event. Rapid-response teams or medical emergency teams are in-hospital emergency teams designed specifically for this purpose. These teams respond to patients on general inpatient units who are at high risk of clinical decompensation and then transfer these children to more acute care areas, with the goal of preventing progression to full cardiac arrest.

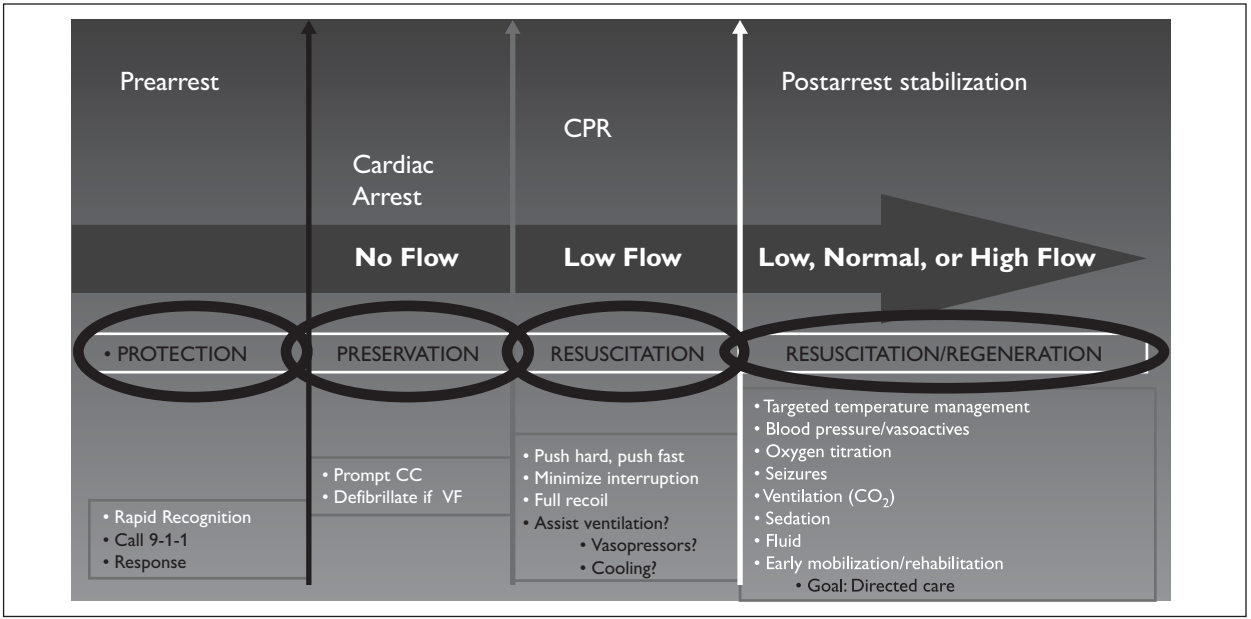

Figure 1.1 Four phases of cardiac arrest and cardiopulmonary resuscitation. CC, cardiac care; CO_2, carbon dioxide; CPR, cardiopulmonary resuscitation; VF, ventricular fibrillation.

No-Flow/Low-Flow Phase

Early recognition and transfer to high-intensity care areas shortens the no-flow phase of untreated cardiac arrest. Attach pads and recognize a shockable rhythm rapidly (ventricular fibrillation [VF] and pulseless ventricular tachycardia). *For each minute of delay in defibrillation of a shockable rhythm, about 7% to 10% of lives are lost per minute*. The pediatric chest compression depth recommendation is at least one-third anterior–posterior chest depth, which is approximately 4 cm in infants and 5 cm in children. After children reach puberty, a depth of at least 5 cm, but no more than 6 cm, is recommended. Effective CPR optimizes coronary and cerebral perfusion pressures and cardiac output to critical organs. Important tenets of basic life support are push hard/push fast, allow full chest recoil between compressions, and minimize interruptions of chest compression. Achieving optimal coronary perfusion pressure, exhaled carbon dioxide concentration, and cardiac output during the low-flow phase of CPR is associated consistently with improved return of spontaneous circulation (ROSC) and improved short- and long-term outcome in both animals and humans. During the low-flow state of CPR, cardiac output and pulmonary blood flow are approximately 25% to 33% of that during normal sinus rhythm; therefore, much less ventilation is necessary for adequate gas exchange from the blood traversing the pulmonary circulation. Near-continuous blood flow is the priority, but adequate oxygenation and ventilation remain important for children because the etiology of most arrests is primarily respiratory compromise. Key common errors during resuscitation include overventilation (e.g., rapid, deep ventilations that increase pressure in the chest and impede venous return to the heart) and long interruptions (e.g., >10 seconds) of chest compressions for rhythm checks, charging of defibrillators, insertion of tracheal tubes, or change of chest compressors who are tiring.

Postarrest Stabilization Phase

The postarrest stabilization phase should focus attention on titration of oxygen, fluids, blood pressure, vasopressors, temperature, glucose, and seizure control in the minutes, hours, and days that follow return of spontaneous circulation. The immediate postresuscitation phase is a high-risk period for ventricular arrhythmias and critical organ (e.g., heart, brain, kidney) reperfusion injuries. The specific phase of resuscitation dictates the focus of care. Note that interventions that improve outcome during one phase may be deleterious during another. For instance, hyperventilation with high pressures and high oxygen may be beneficial during bradycardia with poor perfusion caused by hypoxia and impaired ventilation; but, when pulseless and with CPR in progress, the high pressure and rapid ventilations may impede venous return and decrease

the likelihood of ROSC. Another example is intense vasoconstriction with higher dose epinephrine during the low-flow phase of cardiac arrest improves coronary perfusion pressure and the probability of ROSC; however, that same intense vasoconstriction during the early postresuscitation phase may increase left ventricular wall stress, myocardial strain and dysfunction, and arrhythmia potential.

Medications Used to Treat Cardiac Arrest

No single medication has been shown to improve survival outcome from pediatric cardiac arrest (Table 1.1). The main medication used during cardiac arrest is epinephrine (0.01 mg/kg/dose intravenous [IV] or intraosseous [IO]). Although there are special resuscitation circumstances when other medications such as antiarrhythmics (e.g., amiodarone, lidocaine, adenosine), calcium chloride, and sodium bicarbonate are used, medications are much less important than good circulation and oxygenation/ventilation to impact ROSC and survival outcomes.

Vasopressors

Epinephrine (adrenaline) is the primary resuscitative drug used for cardiac arrest resuscitation. Epinephrine is an endogenous catecholamine with potent α- and β-adrenergic effects. The α-adrenergic action (vasoconstriction) predominates at the doses used for cardiac arrest, which increases systemic, pulmonary, and coronary artery vascular resistance. The resultant increase in aortic diastolic blood pressure improves coronary perfusion pressure and myocardial blood flow, although it may reduce overall cardiac output. Epinephrine also increases cerebral blood flow transiently during CPR. However, evidence suggests that epinephrine can decrease local microcirculatory blood flow at a time when global blood flow is increased. Epinephrine also increases the coarseness of VF, increasing the likelihood of shock success. A study showed that, among

Table 1.1 Medications for Pediatric Resuscitation

Medication	Dose
Amiodarone	5 mg/kg IV/IO; may repeat twice up to 15 mg/kg; maximum single dose, 300 mg
Calcium chloride (10%)	20 mg/kg IV/IO (0.2 mL/kg); maximum single dose, 2 g
Epinephrine	0.01 mg/kg (0.1 mL/kg 1:10,000) IV/IO
Glucose	0.5–1 g/kg IV/IO
Lidocaine	Bolus, 1 mg/kg IV/IO; infusion, 20–50 μg/kg/min
Magnesium sulfate	25–50 mg/kg IV/IO over 10–20 min, faster in torsades de pointes; maximum dose, 2 g
Sodium bicarbonate	1 mEq/kg per dose IV/IO slowly

IO, intraosseous; IV, intravenous.

children with in-hospital cardiac arrest with an initial nonshockable rhythm who received epinephrine, delay in administration of epinephrine more than 5 minutes from time of cardiac arrest was associated with a decreased chance of survival to hospital discharge with a favorable neurological outcome. Note that although high-dose epinephrine (0.05–0.2 mg/kg) can improve myocardial and cerebral blood flow further during CPR and may increase ROSC, administration of high-dose epinephrine can worsen a patient's postresuscitation hemodynamics, and is associated with worse long-term neurological outcome. Thus, high-dose epinephrine is not recommended routinely for either initial or rescue therapy.

Alternative vasopressors, such as the long-acting endogenous hormone vasopressin, act on specific receptors that also mediate systemic vasoconstriction. However, vasopressin has a long half-life and can decrease splanchnic blood flow during and after CPR, and can increase myocardial afterload during the postresuscitation period. Thus, vasopressin is not a first-line agent in pediatric cardiac arrest.

Antiarrhythmic Medications: Lidocaine, Amiodarone, and Magnesium Sulfate

Administration of antiarrhythmic medications should not delay administration of shocks to a patient with a shockable rhythm (VF/ventricular tachycardia). However, after an unsuccessful attempt at electrical defibrillation, medications to increase the effectiveness of defibrillation should be considered. Epinephrine (0.01 mg/kg) is the first-line medication for both pediatric and adult patients in VF. If epinephrine and a subsequent repeat attempt to defibrillate are unsuccessful, lidocaine (1 mg/kg) or amiodarone (5 mg/kg) should be considered. There are limited data and experience with amiodarone use as an antiarrhythmic agent in children. Magnesium sulfate can be given, especially in torsades des pointes, usually in a dose of 50 mg/kg to a maximum of 2 g per dose.

Calcium

In the absence of a documented clinical indication (e.g., hyperkalemia, hypocalcemia, calcium channel blocker overdose, hypermagnesemia), the administration of calcium does not improve outcome from cardiac arrest. For these special resuscitation circumstances, calcium chloride (20 mg/kg/dose) or calcium gluconate (50 mg/kg/dose) is recommended. Despite lack of evidence for efficacy and association with potential harm, calcium is administered frequently during cardiac arrest. Note that routine calcium administration is associated with decreased survival and worse neurological outcomes.

Sodium Bicarbonate

The routine use of sodium bicarbonate is *not* recommended, and is associated with decreased survival and worse neurological outcomes. In special circumstances—such as hyperkalemia, severe acidosis that may depress the

action of catecholamines, tricyclic antidepressant overdose, hypermagnesemia, or sodium channel blocker poisoning—sodium bicarbonate (1 mEq/kg/dose) may be considered. Note also that bicarbonate administration can elevate transiently the arterial and exhaled carbon dioxide load, and should not be used for management of respiratory acidosis.

Medications to Consider for Hyperkalemic Emergency/Cardiac Arrest

Consider the following medications in the following order:

Calcium chloride (10%) 20 mg/kg IV/IO or calcium gluconate 50 to 100 mg/kg IV/IO
Sodium bicarbonate 1 to 2 mEq/kg IV/IO
Glucose 0.5 to 1 g/kg IV/IO
Insulin 0.1 to 0.2 U/kg IV/IO
Albuterol aerosol
Kayexalate (potassium binder) with sorbitol (per rectum)

Postresuscitation Interventions

Targeted Temperature Management

Hyperthermia following cardiac arrest is common in children and is associated with poor neurological outcome. Neonatal trials of selective brain cooling and systemic cooling show promise in neonatal hypoxic–ischemic encephalopathy, suggesting that induced hypothermia may improve outcome. A large multicenter, prospective, randomized study of children age 2 days to 18 years who remained comatose after *out-of-hospital* cardiac arrest found a strong trend but no significant difference in survival with good functional outcome at 1 year and no additional complications in comatose patients who were treated with therapeutic hypothermia (32–34°C) compared with those treated with therapeutic normothermia (36–37.5°C). For infants and children remaining comatose after cardiac arrest, it is reasonable either to maintain 5 days of continuous normothermia (36–37.5°C) or to maintain 2 days of initial continuous hypothermia (32–34°C) followed by 3 days of continuous normothermia. Continuous measurement of temperature during this period is recommended and fever (temperature of 38°C or more) should be prevented and treated aggressively.

Blood Pressure Management

Titrate blood pressure after cardiac arrest to minimize high or low blood pressure during this high-risk period after resuscitation. Small observational

studies after pediatric cardiac arrest show an association of worse survival to hospital discharge when children exhibited hypotension (less than the fifth percentile after ROSC). Maintain a systolic blood pressure of less than the 95th percentile for age. Continuous arterial blood pressure monitoring, with immediate access to inotropes (epinephrine, dobutamine) and vasopressors (epinephrine, norepinephrine), is recommended to identify and treat hypotension rapidly and effectively.

Postresuscitation Myocardial Dysfunction Management

Myocardial dysfunction and arterial hypotension occur commonly after successful resuscitation. The classes of agents used to maintain circulatory function (i.e., inotropes, vasopressors, and vasodilators) should be titrated carefully to the patient's cardiovascular physiology during the postresuscitation phase. Close goal-directed titration, and the use of invasive hemodynamic monitoring, may be appropriate.

Glucose Control

Both hyperglycemia and hypoglycemia after cardiac arrest are associated with worse neurological outcome. There is insufficient evidence to formulate a strong recommendation on the management of hyperglycemia in children with ROSC after cardiac arrest. If hyperglycemia is treated after ROSC in pediatric patients, blood glucose concentrations should be monitored carefully to avoid hypoglycemia, generally with a target glucose range of 80 to 180 mg/dL.

Seizure Surveillance and Control

Seizures are common after cardiac arrest—present in up to 30% of patients. Abnormal electroencephalographic background, burst suppression, and subclinical status epilepticus are all associated with worse neurological outcome. There is no current evidence that seizure prophylaxis or treatment of individual seizures or myoclonus improves outcome. However, close monitoring and treatment of status epilepticus are important postresuscitation goals.

Quality of Resuscitation and Stabilization

The quality of CPR performed during the resuscitation attempt is related directly to patient outcome. Early high-quality CPR is an important determinant of patient survival. The combination of focused bedside training, automated feedback defibrillator, frequent low-dose and high-frequency training, and environmental debriefing can improve guideline compliance, process of care, and outcomes.

Extracorporeal Membrane Oxygenation Cardiopulmonary Resuscitation

Extracorporeal membrane oxygenation cardiopulmonary resuscitation (E-CPR) has been used increasingly as a rescue therapy during CPR, especially for potentially reversible acute postoperative myocardial dysfunction or arrhythmias following cardiac surgery. Studies of E-CPR have demonstrated favorable early survival outcomes in children with primary cardiac disease when E-CPR protocols were in place at the time of the arrest. CPR and extracorporeal membrane oxygenation are not curative treatments. They are simply cardiopulmonary supportive measures that restore tissue perfusion until recovery from the precipitating disease process is achieved. As such, they can be powerful tools. Thus, E-CPR should be considered for children with cardiac arrest who have reversible conditions likely to recover or bridge to transplantation.

Summary

Outcomes from pediatric cardiac arrest and cardiopulmonary arrest events are improving. By focusing therapies strategically to specific phases of cardiac arrest and special, reversible resuscitation circumstances, there is great opportunity for successful cardiopulmonary and cerebral resuscitation in children.

Further Reading

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Chapter 2

Extracorporeal Life Support

Heidi J. Dalton, Mark Davidson, and Peter P. Roeleveld

Extracorporeal membrane oxygenation (ECMO) provides support for several days to weeks as a bridge to recovery or as a bridge to more definitive therapy (e.g., transplant or long-term support) for patients with severe respiratory or cardiorespiratory disease. Roller or centrifugal pumps are used to allow blood to pass from the patient's systemic venous circulation through a gas exchange device or "membrane lung" "before returning to the patient's venous or arterial circulation.

General guidelines and data on patient populations treated and overall outcomes are available on the Extracorporeal Life Support Organization website (www.elso.org). Recommendations can also be found from the Pediatric Acute Lung Injury Consensus Conference.[1] Reasonable criteria for use of ECMO follow.

Criteria for ECMO

1. *Exclusion*: patient for whom life-sustaining treatment is likely to be limited
2. *Inclusion*
    a. *Respiratory failure*
        i. Oxygenation index (OI)
            1. OI = Mean airway pressure × $FiO_2(100)/PaO_2$
            2. Consider ECMO for serial OI more than 25.
            3. OI values at 24 hours and worst in first 24 hours are associated with mortality (e.g., OI >16 at 24 hours is assocated with 28% mortality).
        ii. OI plus alveolar dead space (>30%) may help identify patients at high risk of mortality.
        iii. Mechanical ventilation less than 14 days (Longer duration of prior mechangical ventilation is a relative contraindication)
        iv. Consider P/F ratio less than 50 to 100.
        v. Inadequate gas exchange at conventional ventilator settings (CMV) (PIP <30 cm H_2O; PEEP ≥10 cm H_2O; FiO_2, 1.00)
        vi. Hypercapnia; inability to ventilate (persistent respiratory acidosis, pH <7.20)

vii. Consider high frequency, prone positioning, inhaled nitric oxide. If no response to escalating therapy within a few hours, consider ECMO.
viii. Severe air leak

b. *Cardiac failure/septic shock*
   i. Inability to separate from cardiopulmonary bypass
   ii. Persistent metabolic acidosis, elevated lactate, use of high-dose inotropes
   iii. Use of venoarterial support in patients with aortic dissection or aortic insufficiency is not recommended.

c. *Extracorporeal cardiopulmonary resuscitation: ECMO initiated during cardiac arrest.* Consider involvement of extracorporeal cardiopulmonary resuscitation team after first dose of epinephrine without return of spontaneous circulation.

ECMO system components vary. Common components include the following.

ECMO Systems

1. *Roller pump or semiocclusive pumps* require gravity drainage and a longer circuit than a centrifugal pump. A venous reservoir (bladder or servoregulation system) helps limit negative pressure and hemolysis. Blood advances through the circuit by roller heads compressing tubing in the pump head casing. Prolonged pressure on tubing can lead to rupture. Occlusion of post-pumphead tubing can result in a rapid increase in pressure and tubing rupture.
2. *Centrifugal pumps*: The spinning centrifugal head draws blood into the pump head and dispels it tangentially. Occlusion does not cause high post-pumphead pressure.
   a. Rotation (RPM) generates "suction" force for venous drainage. RPM must be high enough to generate forward flow; blood can drain *backward* from patient if forward flow is insufficient.
   b. Loss of venous return can generate *high* negative pressure (–500 mm Hg) and hemolysis.
   c. Adequate flow is dependent on preload and afterload!
   d. The centrifugal pump head may trap air and emboli, but may instead distribute the air or particulate matter forward to patient. Risk of air emboli leads most centers to use an air detection device.

   Choosing the mode of ECMO depends on a number of patient factors and equipment available.

Decision Tree for Mode of ECMO

Note: The use of ultrasound to establish size and patency of vessels being considered for cannulation may lessen waste of cannulas. Diameter (in millimeters) × 3 = French size (1 French = external diameter of 0.333 mm)

1. *Patient with cardiovascular instability*
    a. Venoarterial (VA) ECMO cannulation is most likely to provide adequate support
        i. If the chest is open, consider placement of cannulas in right atrium and aorta directly
            1. Allows maximal ECMO flow
            2. Bleeding may be greater than with other sites
        ii. Cervical VA ECMO: right internal jugular (RIJ) vein and right carotid artery
            1. Most common site for small infants (<10 kg)
            2. May be used in older patients. Shorter, larger diameter cannulas than are usually possible for femoral vein (FV) cannulation allow better venous return.
            3. There may be a greater risk of stroke higher than with femoral cannulation.
        iii. Femoral VA ECMO: FV and femoral artery (usually >15 kg or >2 years)
            1. Venous cannula
                a. Inserted to IVC/RA junction. A longer cannula adds resistance to flow and may restrict venous return.
                b. Venous engorgement of the limb distal to the cannulation site and compartment syndrome may develop.
            2. Short arterial cannula to limit resistance to flow
                a. Highly oxygenated blood into lower body
                b. In patients with respiratory dysfunction, poorly oxygenated blood ejected from the left heart may perfuse the brain, heart, and upper body preferentially to ECMO flow. Watch for the "red lower body/blue upper body syndrome." Follow arterial oxygen saturation with blood gases from the right radial artery or other means of following upper body saturations.
                c. Venous saturation obtained from the superior vena cava in femoral VA ECMO in patients with severe respiratory disease may be low and may serve as an indicator that additional upper body oxygenation is needed.
                d. Distal limb ischemia with a femoral arterial cannula can occur and demands close monitoring of perfusion
                    i. Place the distal perfusion cannula down the femoral arterial vessel at the time of cannulation and "Y" into arterial return from the ECMO circuit.
                    Or
                    ii. Place the arterial line in the posterior tibial artery and "Y" into the arterial return from the ECMO circuit.
                    iii. Neurovascular compromise can occur even with these methods, requiring amputation.

3. Modified femoral VA ECMO
    a. If there is inadequate upper body oxygen delivery, consider an additional venous cannula into the RIJ vein, "Y-ed" into the *arterial return* from the ECMO circuit. Divert a portion of the arterial blood flow into the RIJ cannula to improve oxygenation of the blood ejected to the upper body from the left heart.
4. Can transition to traditional use of RIJ vein, RIC artery if necessary.

2. *Patients with respiratory dysfunction and hypoxemia or hypercapnia*
    a. May benefit from venovenous (VV) ECMO, with blood withdrawn from and returned into the venous circulation. Adequate native cardiac function is essential.
    b. Common sites
        i. Two-site method:
            1. FV and RIJ vein
                a. Draining from the FV and returning to the RIJ vein limits recirculation.
                b. Cannula tips should be separated by 5 mm or more to reduce recirculation.
                c. Draining from the RIJ vein achieves the best blood flow but allows greater recirculation.
            2. Bilateral FVs
                a. One long and one short cannula helps avoid massive recirculation
                b. Less effective than RIJ vein placement, but good if it is needed for low blood flow only (e.g., hypercapnia)
        ii. Dual-lumen single cannula
            1. *RIJ vein*: Requires careful placement to avoid massive recirculation.
                a. Avalon cannula
                    i. Proper placement at the SVC/RA or IVC/RA sites provides good venous return.
                    ii. Oxygenated return from ECMO is directed toward the tricuspid valve and right ventricle, limiting recirculation.
                    iii. Correct placement is difficult and should be supported with fluoroscopy demonstrating flow from ECMO circuit directed into tricuspid valve.
                    iv. Initial confirmation of placement by echocardiogram (ECHO) can be helpful after cannula positioning.
                b. Other double lumen placement: drains SVC/RA and returns to RA; more recirculation than Avalon, easier to place
        iii. VV ECMO may have fewer neurological complications than VA support.

iv. Patients requiring vasoactive agents before ECMO may tolerate VV ECMO if cardiac dysfunction is secondary to poor oxygenation and/or high intrathoracic pressures.

Once cannulation is complete, ECMO flow is initiated.

Initiation of ECMO

1. Establish initial flow rate goal
   a. Determine cardiac index goal: CO/BSA
   or
   b. Infants: ECMO flow 100 to 150 mL/kg. Single-ventricle physiology and systemic to pulmonary artery shunts may require 200 mL/kg.
   c. Children: 70 to 100 mL /kg ECMO flow
   d. Adults: 50 to 70 mL/kg ECMO flow
   e. Increase flow over approximately 15 minutes. Follow arterial and venous oxygenation, blood pressure, and peripheral perfusion.
      i. Observe ECMO circuit venous return and arterial return pressures.
      ii. Active suction effect of centrifugal heads can create high negative pressure. Most manufacturers provide pressure-drop curves for each cannula across a range of flow rates. Selecting a cannula that provides the expected blood flow at a pressure drop of less than <100 mm Hg is recommended to avoid high negative pressure and hemolysis. Also, exposing the right atrium to pressures more negative than –20 mm Hg can result in damage to the intima. If the venous cannula chosen to provide the expected blood flow rate has a pressure drop of 40 mm Hg from inlet to outlet, the venous servo limit should be set at –60 mm Hg to provide adequate blood flow and to protect the right atrium from damage.
      iii. Arterial line pressures (postpump) are usually maintained at less than 350 mm Hg to prevent hemolysis (and risk of tubing rupture if using roller pump device).
2. When desired venous and arterial saturation levels are achieved, reduce ventilation to rest settings and decrease vasoactive agent dosing as tolerated.
   a. VA ECMO: venous saturation goals, 65% to 75%; arterial saturations, >90% (patient)
   b. VV ECMO: arterial saturations lower than with VA. Arterial saturations more than 80% are desired, but lower saturations may be acceptable if other indicators of adequate oxygen delivery are normal (mentation, hemodynamics, end organ perfusion).
3. Follow routine anticoagulation lab results as well as intermittent lab results for organ function.

Several points specific to ECMO management should be noted.

Special Points: VA ECMO

1. VA ECMO increases left-heart afterload. Inadequate ejection from LV can result in left atrial and pulmonary venous distention, pulmonary edema, and massive pulmonary hemorrhage.
2. Monitor adequacy of forward flow from LV by
   a. Pulse pressure (maintain some pulse pressure during ECMO). Systolic ejection indicates aortic valve opening and LV working; ECMO flow, itself, is usually nonpulsatile.
   b. ECHO provides evidence for aortic valve opening, ejection from LV, LV performance, LA dilation
   c. Chest X-ray to assess presence of pulmonary edema
   d. Suctioning frothy pulmonary edema is an ominous sign if present as a new finding.
3. If LV forward flow is inadequate
   a. Afterload reduction or low-level inotropy may help
   b. Establish drainage of left heart
      i. Closed-chest patients usually require atrial balloon septostomy in cardiac catheterization lab, which allows venous cannula to drain right and left atria.
      ii. Open-chest patients may benefit from placement of direct left-atrial vent catheter and "Y" into venous return to decompress LA.
      iii. In patients with adequate pulmonary gas exchange, ECMO circuit venous saturation is increased by oxygenated blood from the native pulmonary veins/left atrium mixing with the venous return to the pump. Need to use venous saturation at a site not "contaminated" with left-heart return (e.g., femoral venous catheter).
4. Vessel reconstruction at decannulation (especially carotid and femoral artery) is often recommended, but data on long-term benefit are limited.

Special Points: VV ECMO

Concerns specific to ECMO management are noted in this section.

1. Recirculation
   a. Occurs when oxygenated blood returning from the ECMO circuit is drawn back into the drainage cannula without reaching the patient's systemic circulation.
   b. Results in high-circuit SvO_2 but limits systemic oxygenation.
   c. Can highlight cannula malposition.
   d. Impact of recirculation
      i. New signs of impaired oxygen delivery

ii. Increased ECMO flow increases circuit SvO_2 without an increase in patient's SaO_2
iii. On occasion, reducing ECMO flow decreases recirculation.

Special Points: Specific Cardiac Lesions

Management of patients with congenital heart defects on ECMO requires recognition of specific physiology.

1. Single-ventricle patients
   a. Initially, during full ECMO support, target normal arterial saturation.
   b. As the myocardium recovers and ECMO is weaned, saturations will decrease as the patient's mixed circulation becomes the predominant source of blood flow.
   c. Clipping the Blalock-Taussig shunt is not recommended unless pulmonary blood flow during ECMO is excessive and limits systemic flow. Clipping may be associated with lung ischemia, reperfusion injury, and increased risk of death.
2. ECMO may be considered in patients with a bidirectional Glenn or Fontan circulation with profound low cardiac output after excluding obstruction in the bidirectional Glenn or Fontan circuit. Outcome in these patients is inferior compared with other cardiac lesions supported with ECMO. A patient may require both SVC and IVC drainage.

Patient Management during ECMO

Although patient care must be individualize, some generally accepted elements of management follow.

1. *Ventilator settings*
   a. Reduce to "nontoxic" settings (e.g., PEEP, 5–15 cm H_2O; PIP, <25–30 cm H_2O; rate, 6–10; FiO_2, 0.21–0.5) *or* promote spontaneous breathing with pressure support or similar mode.
      i. Consider early tracheostomy if ECMO course likely to be prolonged.
      ii. Extubation is possible in both cardiac and respiratory failure patients.
   b. Dyspnea during weaning is common even with adequate pCO_2 and arterial oxygen saturations. If patient can tolerate changes, proceed with weaning.
   c. Expect low tidal volumes in patients with acute respiratory distress syndrome and poor compliance (e.g., 1–3 ml/kg). *Do not* increase vent settings to "recruit" poorly compliant lungs; await lung healing, which may take weeks.

2. *Prone positioning* may be done safely, but is not routine.
3. *Bronchoscopy* may be useful to assess pathology but should not be routine.
4. *Inotropes*: wean inotropic support as tolerated.
5. *Infection*: There is no indication for prophylactic antibiotics in patients on ECMO. Markers of blood stream infections, such as temperature lability and inflammatory markers are unreliable. Cultures for suspected infection and appropriate treatment should be instituted as needed.
6. *Renal*: Renal failure is associated with increased mortality. Almost all patients on ECMO receive diuretics. Renal replacement therapy to maintain fluid balance or support renal insufficiency via a hemofilter placed in an ECMO circuit or via conventional renal replacement therapy devices is recommended.
7. *Nutrition*: Nutritional support is essential. Most patients tolerate enteral nutrition.
8. *Pharmacology*: When therapeutic drug level measurements are available, they should be done to demonstrate adequate dosing.
9. *Neurology*: Baseline head ultrasound in neonates and serial examinations for the first few days of ECMO are recommended to identify bleeding or infarction. Keeping patients awake to monitor neurological status is optimal.
10. *Anticoagulation*: Heparin is the agent used most commonly. A bolus dose of 50 to 100 U/kg at cannulation is routine, followed by a continuous infusion (10–20 U/kg/h) after the anticoagulation goal is reached (activated clotting time, <300 seconds).
11. *Monitoring*:
    a. Activated clotting time: range, 160 to 220 seconds. Can be done at bedside.
    b. Anti-Xa: 0.30 to 0.7 U/mL. Usually checked every 4 to 8 hours or less.
    c. PTT: 1.5 to 2 times normal (not very reliable in neonates)
12. *Alternatives to heparin*:
    a. Argatroban (adapted from University of Michigan ECLS program)
        i. Dosing: 0.2 µg/kg/min and increase; maximum level, 10 µg/kg/min. Increase by 0.05 µg/kg/min every 45 minutes as needed.
        ii. Monitoring: aPTT, 1.5 to 2.5 normal.
    b. Bivalirudin (250 mg + sodium chloride 0.9% 250 mL) (adapted from Mayo Clinic ECLS program)
        i. Give IV 0.15 mg/kg/h. May start at 0.05 mg/kg/h if worried about bleeding.
        ii. Monitor via aPTT 1.5 to 2.5 normal
        iii. Adjust drip as follows:
        iv. aPTT less than goal: Increase infusion rate by 20%; recheck aPTT in 2 hours.
        v. aPTT within goal range: No change in infusion; recheck aPTT in 2 hours. If still within therapeutic range, may check aPTT every 12 hours to daily.

vi. aPTT more than goal: *Stop* infusion for 1 hour, then decrease infusion rate by 30%; recheck aPTT in 2 hours.

13. *Blood product replacement* (adapted from St. Louis Children's Hospital, with permission):
    a. Packed red blood cells (10–20 cc/kg) to maintain hemoglobin (usually 7–10 g/dL)
        i. Patients with impaired oxygenation on VV support may benefit from increased hemoglobin to increase oxygen carrying capacity.
    b. Platelets: 10–20 mL/kg; maximum, usually 2 U at a time
        i. Nonbleeding patient
            1. Maintain more than 100,000 if at high risk of intracranial bleeding.
            2. Maintain more than 50,000 if not at high risk of intracranial bleeding.
            3. In patients with persistent thrombocytopenia, assess for heparin-induced thrombocytopenia. If a result of a chronic condition, accept lower platelet count (levels 20,000–50,000 reported without bleeding).
        ii. Actively bleeding patient: usually maintain platelet count more than 100,000
    c. Fresh frozen plasma: 10–20 cc/kg; maximum, usually 2 U
        i. Nonbleeding patient: INR more than 2, reduce heparin dose if tolerated, consider FFP.
        ii. Bleeding patient: INR more than 1.7, reduce heparin dose if tolerated, consider FFP.
    d. Cryoprecipitate: 1 U/10 kg; maximum, 10 U
        i. Maintain fibrinogen more than 100.
    e. Massive bleeding: Follow massive transfusion protocol.
    f. Antithrombin III
        i. Replace if patient has required increasing heparin with little effect, significant thrombotic events, low anti-Xa levels.
        ii. Strict level not known, usually more than 50%.
        iii. Dosage (not well-validated in children):

$$\text{Bolus dose} = \left(\frac{\text{Goal} - \text{Measured activity}}{\text{Goal activity}} \right) \times \text{Total plasma volume}$$

14. *Recovery from underlying disease*:
    a. Evidenced by
        i. Improved cardiac performance via ECHO at lowered flows
        ii. Improved hemodynamic function
        iii. Improved gas exchange (PaO_2, $ETCO_2$) at constant ventilator settings, ECMO flow and FiO_2
        iv. Improved tidal volume and lung compliance, improving CXR

15. *Weaning from VA ECMO*:
    a. Procedure
        i. Increase ventilator settings to ones desired for removal from ECMO
            1. PIP, less than 28; PEEP, 5 to 10; rate appropriate for age; FiO_2, 0.5 or less
            2. Removal of patients from ECMO on no ventilator support is possible but uncommon.
        ii. Decrease ECMO circuit flow by 20 to 50 mL/min (faster if tolerated) to "idle" settings (at least 10 mL/kg/min). Follow hemodynamic function, acid–base status, gas exchange.
            1. If using centrifugal pump and hollow-fiber membrane lung, note that minimal flows (250–500 cc) increase risk of thrombosis/hemolysis. Consider increasing anticoagulation.
            2. Once at "idle" flow, clamp off VA circuit to obtain true "test" of cardiac and pulmonary performance. Need to assess patient gas exchange (especially CO_2 elimination) completely off support because even minimal ECMO flow removes CO_2 very efficiently. During clamped period, must reestablish flow through cannulas every 10 minutes to prevent clotting.
            3. Obtaining ECHO at low flow or clamped ECMO helps to assess cardiac function.
            4. If patient is hemodynamically stable with adequate gas exchange for 1 to 2 hours, decannulation may be indicated.
16. *Weaning from VV ECMO*:
    a. Procedure
        i. Increase ventilator settings as noted earlier.
        ii. Decrease FiO_2 and gas flow to oxygenator, and "cap" it by removing gas inflow line so that no CO_2 is removed or oxygen is added.
        iii. Because all blood flow is withdrawn and returned to the venous circulation, weaning ECMO flow is not essential, but decreasing flow gradually may help "condition" the heart to assume normal cardiac output and ventricular configuration. Maintaining adequate circuit flow to prevent thrombosis is essential. Total clamping off ECMO with VV support is *not* needed.
        iv. Monitor hemodynamic function and gas exchange.
        v. Decannulate if hemodynamic function and gas exchange are stable.
17. *Special points during weaning*:
    a. If patient has a left atrial vent, it must be clamped or removed to allow left heart filling during weaning.
    b. If patient has an atrial communication created during ECMO, filling the native ventricle at reduced ECMO flows (VA ECMO) may induce a right-to-left atrial shunt (or vice versa). Closure of the atrial communication after ECMO or, rarely, during ECMO before successful weaning may be necessary.