Parallel Circulations: Managing Single-ventricle Physiology

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Parallel Circulations:
Managing Single-ventricle Physiology

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Author Disclosure
Drs Mastropietro and Tourner have disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

Objectives
After completing this article, readers should be able to:

1. Review the unique anatomy and physiology of patients born with a single cardiac ventricle.
2. Understand why this unique anatomy and physiology requires a physiologic approach to cardiopulmonary resuscitation.

Abstract
Infants born with single-cardiac ventricle physiology frequently are treated preoperatively and postoperatively in neonatal intensive care units (NICUs), which requires neonatologists to be familiar with their unique anatomy, physiology, and consequent nonconventional principles of management. This case report reviews single-ventricle anatomy and physiology to explain appropriate interventions in the setting of cardiopulmonary arrest.

Introduction
Approximately 170 per 100,000 live births involve critical congenital heart disease, defined as conditions that are ductal-dependent or require surgical or interventional attention in the first postnatal month. (1) Many affected infants have defects that result in only one functional cardiac ventricle, such as tricuspid atresia with hypoplastic right heart or the classic hypoplastic left heart syndrome. The single ventricle pumps blood to both the pulmonary and systemic circulations in parallel and requires the ductus arteriosus for pulmonary or systemic blood flow. Surgical palliation frequently is performed shortly after birth. The ductus arteriosus is ligated and a more secure systemic-to-pulmonary artery shunt is placed to maintain adequate blood flow to both circulations until further palliation procedures can be performed. Because neonates who have critical congenital heart disease frequently are treated preoperatively and postoperatively in the NICU, neonatologists should be familiar with their unique anatomy and physiology as well as the appropriate principles of management, especially in the setting of an acute cardiopulmonary arrest.

Case Study
A term female infant who had an antenatal diagnosis of pulmonary atresia with intact ventricular septum and severe right ventricular hypoplasia (Fig. 1) is admitted to the NICU. She is started immediately on prostaglandin E_1 (PGE_1) infusion to maintain patency of the ductus arteriosus and ensure adequate pulmonary blood flow. She remains stable in the NICU, with oxygen saturations, as determined by pulse oximetry (Spo_2), of 75% to 85% while awaiting surgical palliation.

Pathophysiology
The congenital heart defect described for this infant is an example of single-ventricle physiology, in which the left ventricle pumps blood to the pulmonary and systemic circulations. Other examples of single ventricle lesions are

Abbreviations
NEC: necrotizing enterocolitis
NICU: neonatal intenstive care unit
PGE: prostaglandin E
PVR: pulmonary vascular resistance
Spo_2: oxygen saturation as determined by pulse oximetry
SVR: systemic vascular resistance

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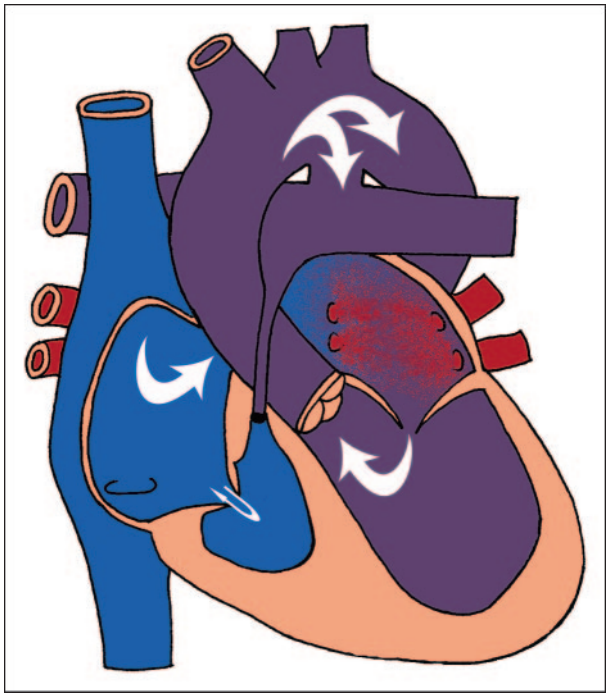

Figure 1. Pulmonary atresia with intact ventricular septum (PA/IVS) preoperatively. Due to a hypoplastic right heart, deoxygenated blood returning to the right atrium must traverse an obligate atrial septal defect, mix with oxygenated blood returning to the left atrium from the lungs, and enter the left ventricle, where it is pumped to both circulations. Pulmonary blood flow is maintained through the open ductus arteriosus.

listed in Table 1. As demonstrated in Figure 1, deoxygenated blood returning to the heart from the systemic veins enters the right atrium, traverses an obligate atrial communication, and mixes with oxygenated blood entering the left atrium from the pulmonary veins. This admixture enters the left ventricle, where it is pumped into the ascending aorta. In the aorta, a portion of the stroke volume crosses the ductus arteriosus to supply the pulmonary circulation; the remainder continues through the descending aorta to perfuse the systemic arterial tree. This infant has one ventricle supplying two circulations with ductal-dependent pulmonary blood flow. PGE_1 initiated immediately after delivery can maintain patency of the ductus arteriosus and preserve pulmonary blood flow. (2)(3)

Blood ejected by the left ventricle is composed of deoxygenated systemic venous blood and oxygenated pulmonary venous blood, resulting in systemic arterial oxygen saturation (Sao_2) that always is less than 100%. Clinically, Spo_2 is used routinely as a surrogate marker of Sao_2. Sao_2 is determined by the relative proportions of oxygenated and deoxygenated blood. If systemic venous return is markedly greater than pulmonary venous return, the patient is more desaturated and vice versa. The proportions of venous return depend on how much blood flows to the pulmonary circulation through the ductus arteriosus compared with that entering the systemic circulation through the aorta. This ratio is referred to as the Q_p:Q_s, where Q_p is pulmonary blood flow and Q_s is systemic blood flow. The ideal Q_p:Q_s is 1, which is present when the circulations are perfectly balanced, similar to an anatomically normal heart, where the pulmonary and systemic circulations are in series. The patient who has a single ventricle and a Q_p:Q_s of 1 generally has Sao_2 measurements of 75% to 85%. (4) The proportion of blood entering each circulation depends on the resistance of each circulation. If pulmonary vascular resistance (PVR) is higher than systemic vascular resistance (SVR), more blood preferentially enters the systemic circulation. Pulmonary blood flow and pulmonary venous return are decreased, resulting in a decreased Sao_2, typically less than 75%. In contrast, if PVR is less than SVR, blood preferentially enters the pulmonary circulation via the ductus arteriosus. The proportion of pulmonary blood flow and oxygenated pulmonary venous return is greater than systemic blood flow and deoxygenated systemic venous return, resulting in highly oxygenated blood. More importantly, pulmonary blood flow is increased at the expense of systemic blood flow, including cerebral, splanchnic, and coronary flow. Such undesirable physiology is reflected by Sao_2 measurements of more than 85%.

Stimuli for pulmonary vascular dilatation, such as hyperoxia and alkalosis, decrease PVR and promote pul-

Table 1. Congenital Heart Defects With Single-ventricle Physiology

Single Left Ventricle

- Tricuspid atresia
- Pulmonary atresia with intact ventricular septum
- Severe Ebstein anomaly
- Double-inlet left ventricle
- Left ventricle-dominant atrioventricular canal

Single Right Ventricle

- Mitral atresia with hypoplastic left heart syndrome
- Mitral atresia with double-outlet right ventricle
- Aortic atresia with hypoplastic left heart syndrome
- Right ventricle-dominant atrioventricular canal

monary blood flow at the expense of systemic perfusion. Unless concomitant respiratory disease is present, infants should be treated in room air. If SaO_2 remains more than 90% in room air, the dose of PGE_1 may need to be decreased to regulate pulmonary blood flow by limiting the size of the ductus arteriosus. Systemic afterload reducers such as the phosphodiesterase III inhibitor milrinone (0.375 to 0.75 mcg/kg per minute) and the angiotensin-converting enzyme inhibitor enalapril (0.1 to 0.5 mg/kg per day divided BID) decrease SVR, improving systemic blood flow. Accordingly, increases in SVR, which augment pulmonary blood flow and further hinder systemic perfusion, must be avoided. Agitation and pain should be minimized, and drugs that cause systemic vasoconstriction (eg, high-dose dopamine or epinephrine, norepinephrine, vasopressin, phenylephrine) should be used with extreme caution. In cases where SaO_2 remains greater than 90% despite measures to increase PVR and lower SVR, mixtures of nitrogen or carbon dioxide with oxygen to create subambient FiO_2 (eg, 15% to 20%) can be administered to increase PVR.

Case Continuation

On the ninth postnatal day, the infant undergoes placement of a 4-mm modified Blalock-Taussig shunt and ligation of the ductus arteriosus without complications (Fig. 2). Despite breathing room air, her SpO_2 is consistently 90% to 95% postoperatively, suggesting excessive pulmonary blood flow, potentially at the expense of systemic blood flow. Enalapril is initiated, after which her SpO_2 decreases to 85% to 90%. Shortly thereafter, she is discharged 16 days after birth.

Surgical Treatment

Infants who have single-ventricle physiology typically undergo surgical placement of a systemic-to-pulmonary shunt in the first few weeks after birth, eliminating dependency on the ductus arteriosus and allowing discontinuation of PGE_1 infusion. Patients who have insufficient **left** ventricles, such as those who have hypoplastic left heart syndrome. often have diminutive or atretic aortas, necessitating both a shunt and the Norwood procedure. In the Norwood procedure, the main pulmonary artery trunk is transected from the branch pulmonary arteries and used to reconstruct the hypoplastic aortic arch, creating a neo-aorta. Because the size of the aortas in most patients who have hypoplastic **right** ventricles is adequate, such as for this patient, they generally only require shunts. The most common shunt used in both patient populations is the modified Blalock-Taussig shunt, in which a polytetrafluoroethylene (Gore-Tex®) graft is interposed between the subclavian or innominate

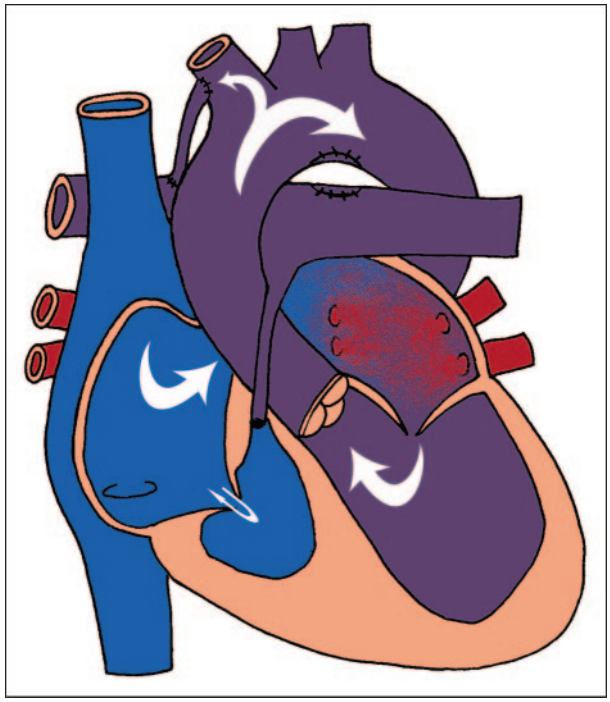

Figure 2. PA/IVS following placement of a Blalock-Taussig shunt and ligation of the ductus arteriosus. Pulmonary blood flow no longer is dependent on the ductus arteriosus; rather, some of the blood ejected into the aorta enters the pulmonary circulation via the shunt, which connects the right subclavian artery to the right pulmonary artery.

artery and ipsilateral pulmonary artery (Fig. 2). Pulmonary blood flow is dependent on this connection.

In the immediate postoperative period, the Q_p:Q_s is monitored closely to ensure adequate end-organ perfusion. Optimal end-organ function and improved survival rates correlate with a Q_p:Q_s between 1 and 2, which corresponds to an SaO_2 of 75% to 85%. (5) The Q_p:Q_s can be calculated using the Fick principle, in which total consumption of oxygen is equal to the product of the blood flow and the arterial-venous oxygen concentration difference: (6)

$Q_p/Q_s = SaO_2\text{-}SvO_2/SpvO_2\text{-}SpaO_2$

Q_p: pulmonary blood flow
Q_s: systemic blood flow
SaO_2: aortic saturation
SvO_2: mixed venous saturation
$SpvO_2$: pulmonary venous saturation
$SpaO_2$: pulmonary artery saturation

To calculate Q_p:Q_s, several assumptions are made. First, in single-ventricle lesions, pulmonary arterial oxygen saturation ($SpaO_2$) should be equivalent to systemic arterial oxygen saturation (SaO_2) because blood supply to

Table 2. Calculation of Qp:Qs in Single-ventricle Physiology

O_2 saturation	Sao_2/Svo_2*	$Spvo_2/Spao_2$	Q_p/Q_s	$Q_p:Q_s$
75%	75/50	100/75	25/25	1
85%	85/60	100/85	25/15	1.7
95%	95/70	100/95	25/5	5

*Svo_2 values used assume normal oxygen consumption and extraction. In practice, the actual measured values of Svo_2 obtained from the SVC should be used. Q_p=pulmonary blood flow, Q_s=systemic blood flow, Sao_2=aortic saturation, Svo_2=mixed venous saturation, $Spvo_2$=pulmonary venous saturation, $Spao_2$=pulmonary artery saturation

the pulmonary artery and the aorta are derived from the single ventricle. Pulmonary venous oxygen saturation ($Spvo_2$) can be assumed to be 100% in the absence of significant lung disease. Mixed venous oxygen saturation (Svo_2) is measured by sampling blood from a central venous catheter with the tip in the superior vena cava, the accepted method of measuring Svo_2. (7) Under circumstances of normal oxygen consumption and extraction, the difference between arterial and mixed venous oxygen saturations is 25% to 30%. Using these assumptions, Q_p:Q_s can be estimated (Table 2). It is evident that as the aortic oxygen saturation increases, the Q_p:Q_s increases disproportionately. Aortic oxygen saturation of 95% represents a pulmonary flow five times the volume of systemic flow. For patients who have single-ventricle physiology, an Sao_2 greater than 90%, whether measured directly from arterial blood or indirectly with pulse oximetry, is a state of pulmonary overcirculation and systemic hypoperfusion.

The diameter of a Blalock-Taussig shunt typically is either 3.5 mm or 4.0 mm, depending on the size of the infant. (6) The resistance of the shunt, which is primarily dependent on the diameter, should be greater than PVR and result in an optimal Q_p:Q_s. Moreover, because the resistance of the shunt is fixed, as long as the shunt provides appropriate restrictive flow to the pulmonary circulation, interventions to decrease SVR no longer should be necessary. The infant is not susceptible to stimuli that would increase pulmonary blood flow.

In this infant, the Sao_2 was more than 90% following shunt placement, suggesting that the 4.0-mm shunt likely was providing insufficient resistance to pulmonary blood flow, allowing too much pulmonary blood flow and compromising systemic blood flow. In this clinical scenario, manipulating SVR and PVR becomes relevant. Enalapril was effective in lowering SVR in the immediate post-operative period.

Case Continuation

At age 21 days, the infant presents to the emergency department after two episodes of bright red blood with stooling. No history of fever, irritability, difficulty feeding, tachypnea, sweating, or cyanosis is present. Her abdominal radiograph, however, is suspicious for necrotizing enterocolitis (NEC). She is readmitted to the NICU for medical management of NEC (ie, NPO, broad-spectrum antibiotic therapy). On admission, her temperature is 98.8°F (37.1°C), heart rate is 160 beats/min, blood pressure is 81/35 mm Hg, respiratory rate is 40 breaths/min, and Spo_2 is 89% on room air. On hospital day 2, she becomes increasingly agitated during her bath, then suddenly develops apnea. Her heart rate decreases from 140 to 150 beats/min to 70 to 80 beats/min, and she has cool extremities and weak pulses. Spo_2 is nondetectable. She is promptly endotracheally intubated, provided bag-valve ventilation with an inspired oxygen concentration of 100%, and given one dose of epinephrine 10 mcg/kg intravenously, which results in no improvement. She develops more severe bradycardia, and pulses no longer are palpable. Chest compressions are initiated, and a second dose of epinephrine is administered without improvement. About 5 minutes after the initial apneic episode, her heart rate is 24 beats/min and she is pulseless. At this time, her resuscitation bag is disconnected from the oxygen source, decreasing the inspired oxygen concentration to 21%. Concomitantly, a 10-mL/kg bolus of 0.9% saline is administered, after which the heart rate quickly increases to 150 to 160 beats/minute and pulses become palpable.

Potential Complications

Patients who have single-ventricle physiology are extremely fragile. Hypoxemia (Sao_2<75%) in those who have single-ventricle anatomy with a shunt is particularly ominous because it could be caused by pulmonary venous desaturation due to lung disease, decreased pulmonary blood flow due to shunt stenosis or thrombosis, or systemic venous desaturation due to low cardiac output. (6) In the last scenario, as cardiac output decreases, the Svo_2 also decreases as more oxygen is extracted. Because Sao_2 in single ventricle depends on blood return to both the right atrium and left atrium, a decrease in Svo_2 decreases Sao_2, leading to a vicious cycle of desaturation. Although exogenous oxygen is indicated for pulmonary venous desaturation and shunt occlusion, it is contraindicated for patients who have low cardiac output. If the shunt is large, exogenous oxygen increases Sao_2 by increasing pulmonary blood flow but decreases systemic cardiac output by diverting blood away from the systemic circuit. In these patients, oxygen delivery to vital organs

is improved by optimizing preload (ie, volume), minimizing afterload (ie, milrinone), and increasing contractility and heart rate (ie, inotropes).

Hypoxemia was not an issue in this patient. Her Sao_2 on admission was mildly elevated, suggesting the possibility of episodic pulmonary overcirculation with consequent systemic, including splanchnic, hypoperfusion at home, leading to the development of NEC. She was stable on minimal support in the NICU until her sudden cardiac arrest. Agitation produces a surge of endogenous catecholamine release from the sympathetic nervous system, increasing SVR. This patient's sudden cardiac arrest likely was precipitated by such a "sympathetic surge," at which time most of the blood ejected from the single ventricle was directed into the pulmonary circulation through the large shunt. More importantly, the blood was diverted away from the systemic circulation. Coronary blood flow was compromised and bradycardia ensued. Endotracheal intubation always is warranted in this situation, but neonates who have single-ventricle physiology, especially those prone to pulmonary overcirculation, should not receive an inspired oxygen concentration of 100% unless pulmonary disease and consequent pulmonary venous desaturation are suspected. This patient did not have pulmonary disease and, thus, an inspired oxygen concentration of 100% exacerbated the problem by decreasing PVR, diverting additional blood flow into the lungs and away from the systemic circulation, and likely decreasing coronary arterial flow. In this clinical scenario, because epinephrine increases SVR, its ineffectiveness during resuscitation is not surprising. Fortunately, appropriate therapy was initiated when the Fio_2 was reduced to 0.21 through the endotracheal tube, thereby increasing PVR, improving coronary blood flow, and restoring spontaneous rhythm. The fluid bolus was also helpful, concomitantly improving preload, which augmented stroke volume and coronary blood supply.

Case Conclusion

Over the next few hours, although receiving mechanical ventilation with an inspired oxygen concentration of 21% and starting milrinone at 0.5 mcg/kg per minute, the infant's Spo_2 remains at 92% to 97%. Exogenous nitrogen is added and the inspired oxygen concentration is titrated down to 16%, at which point the Spo_2 is 85%. Cardiac catheterization performed 48 hours later does not reveal any abnormal coronary artery anatomy that could explain the acute deterioration. This course confirms the diagnosis of systemic hypoperfusion due to excessive shunt flow to the pulmonary circulation. To wean her from subambient Fio_2, she returns to the operating room for banding of her shunt. In this procedure, the diameter of the shunt is reduced to create a higher fixed resistance to blood flow. After the procedure, her inspired oxygen concentration is titrated to 21%, with Spo^2 values remaining at 75% to 85%. She is discharged on enalapril with no further complications.

Conclusion

Advances in pediatric cardiovascular surgery have dramatically increased the survival of neonates with single-ventricle physiology. Neonatologists must be familiar with this unique anatomy and physiology to provide appropriate care. The ideal Sao_2 values of 75% to 85% for these patients represent a Q_p:Q_s of 1 to 2 and should not result in systemic hypoperfusion. Attempts to increase Sao_2 further are not beneficial. In the setting of cardiopulmonary arrest in an infant who has single-ventricle physiology, oxygen must be used cautiously. In the absence of pulmonary disease or shunt occlusion, an inspired oxygen concentration greater than 21% rarely is needed and can be detrimental.

American Board of Pediatrics Neonatal-Perinatal Medicine Content Specification

- Know the evaluation and management plans (medical and/or surgical) and associated potential complications or adverse effects of such management for a neonate with a left-sided cardiac obstructive lesion.

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NeoReviews Quiz

10. In newborns who have single-ventricle physiology, the proportions of venous return depend on how much blood flows to the pulmonary circulation through the ductus arteriosus compared with that entering the systemic circulation through the aorta. Ideally, the pulmonary blood flow (Q_p) and systemic blood flow (Q_s) should be balanced, leading to a Q_p:Q_s ratio of 1.0 to 1.7, which corresponds to a systemic oxygen saturation (Sao_2) of 75% to 85%. If the Sao_2 remains unacceptably high (>90%), therapeutic measures to increase pulmonary vascular resistance and lower systemic vascular resistance are warranted. Of the following, the therapeutic measure *most* likely to improve systemic blood flow in infants who have single-ventricle physiology is administration of:

    A. Arginine-vasopressin.
    B. High-dose dopamine.
    C. Phosphodiesterase III inhibitor milrinone.
    D. Sodium bicarbonate.
    E. Supplemental oxygen.

11. Infants who have single-ventricle physiology typically undergo surgical placement of a systemic-to-pulmonary shunt in the first few weeks after birth, eliminating dependency on the ductus arteriosus and allowing discontinuation of prostaglandin infusion. Of the following, the *most* common procedure, pioneered by Blalock and Taussig, used in affected infants involves shunting of the:

    A. Ascending aorta to right pulmonary artery.
    B. Descending aorta to left pulmonary artery.
    C. Subclavian artery to ipsilateral pulmonary artery.
    D. Superior vena cava to right pulmonary artery.
    E. Transverse aorta to pulmonary artery.

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