SINGLE VENTRICLE PHYSIOLOGY EPISODE 2: HYPOPLASTIC LEFT HEART SYNDROME

Developed by Dr. Sabine Laguë and Dr. Shreya Moodley for PedsCases.com.
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Introduction:

Hello, my name is Sabine Laguë and I am a 1st year pediatrics resident at the University of British Columbia in Vancouver, Canada. I am joined on this podcast today by Dr. Shreya Moodley, a pediatric cardiologist at BC Children's Hospital in Vancouver. I would like to thank Dr. Moodley for her guidance in putting together this podcast, as well as PedsCases.com for their constructive feedback on the script and for this exciting avenue to discuss this interesting topic.

This is the second of three episodes in a series on single ventricle physiology. We are very excited about this series because now more than any time in history we are seeing an increasingly growing number of individuals living and thriving into adulthood with single ventricle physiology post-Fontan palliation. Regardless of the type of medicine you are currently or will end up practicing, it is possible that you will end up working with individuals from this population. Thus, an awareness of Fontan physiology and the systemic complications of this circulation is important.

This second episode discusses hypoplastic left heart syndrome (HLHS), a common form of single ventricle physiology. The first episode focused on tricuspid atresia, another relatively common form of single ventricle anatomy. Both episodes follow the patient from birth through to childhood. The third episode revisits both of these patients in their late adolescence and discusses long-term management and complications of patients post-Fontan.

Please see the script on the Pedscases website for helpful figures and diagrams to help you better understand the underlying cardiac physiology. These are also referenced in the show notes.

The objectives of this podcast are to:

1. Describe hypoplastic left heart syndrome (HLHS), its underlying pathology and pathophysiology, and its associated anomalies.
2. Discuss common presenting symptoms and physical exam findings of a patient with HLHS.

3. Outline modalities used to diagnose and monitor HLHS both antenatally and postnatally.
4. Discuss initial medical management of a neonate with HLHS.
5. Diagram the three stages of surgical management and distinguish their unique purpose in surgical palliation.

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You're a 3rd year medical student on your pediatric cardiology rotation and the fellow that you are on call with receives a phone call from a family doctor in rural British Columbia.

The family doctor tells you both about Olivia, a 3 day old previously well full-term newborn girl, who was brought to the emergency department cyanotic, diaphoretic, and tachypneic, with nasal flaring, and significant subcostal and suprasternal retractions. There was limited prenatal care during the pregnancy and due to socioeconomic barriers her mother was unable to access her 20-week standard anatomical obstetrical screening ultrasound. Olivia was born at the rural community hospital at 40 weeks gestation via an uncomplicated spontaneous vaginal delivery. Her newborn exam was normal. They were discharged from hospital 12 hours post-delivery and did not undergo the routine newborn screening, including congenital heart disease pulse oximetry screening.

Olivia was well for the first 2 days of life. She was feeding and producing wet diapers. Today however she became increasingly diaphoretic with feeding and over the last few became lethargic and "not her normal self", which is why her mother brought her to the emergency department.

On physical exam, the family physician noted that Olivia looked sick. She was tachypneic and tachycardic with cyanosis and poor peripheral pulses. She was tired, but rousable. Based on the history and physical exam, the family doctor suspected congenital heart disease. You and the cardiology fellow, upon hearing this, arrange for the infant to be transported to the children's hospital and provide some guidance for immediate management.

* * *

As the fellow is making the arrangements for transport, you recall that congenital heart disease is relatively prevalent, making up approximately 1% of the general population, or 8-12 of every 1000 live births.[1]

The fellow helps to stabilize Olivia over the phone and asks if there is IV access. The fellow suggests starting prostaglandin. A chest x-ray and ECG are being sent to you.

While you are waiting for the patient to arrive, you review potential causes of cyanosis with the fellow.

Student: Can you walk me through your approach to the different causes of cyanosis?

Fellow: I like to start by breaking it down into whether it is central cyanosis, peripheral cyanosis, or methemoglobinemia. Central cyanosis is the reduction in arterial oxygen saturation. If it is central cyanosis, we then need to determine whether or not the etiology is respiratory or cardiac. To differentiate the two we use a hyperoxia test. First, perform an arterial blood gas, then give the patient 100% oxygen for 10 minutes, and repeat the arterial blood gas. In a patient with congenital heart disease the P_aO_2 may rise slightly, but it will not rise above 100 mmHg. If it does rise above 100 mmHg, then the underlying cause of the central cyanosis is respiratory. Peripheral cyanosis is an increase in deoxygenation at the level of the capillaries, which is most commonly seen in acrocyanosis in newborns, but can also be seen in circulatory shock and congestive heart failure. Finally, always consider methemoglobinemia, which can be either congenital or acquired. In this condition it is difficult for the oxygen to be effectively released to the tissues.

A few hours later the patient arrives to the Children's Hospital and is transferred to the cardiac ICU. The patient is stabilized and an echocardiogram is performed. The diagnosis is confirmed as hypoplastic left heart syndrome or HLHS.

Fellow: Can you tell me more about HLHS?

Student: HLHS is the hypoplasia of the left ventricle with associated critical stenosis or atresia of the mitral and/or aortic valve, as well as the aorta itself.[2] It makes up 4-8% of congenital heart disease diagnoses.[3]

Fellow: That's correct.

*The fellow grabs a piece of paper and draws out a heart with normal cardiac anatomy **(Figure 1A)** and a heart with HLHS (**Figure 1B**).*

Fellow: HLHS is characterized by a spectrum of underdeveloped left-sided cardiac structures, dominant right ventricle and systemic outflow tract obstruction not amenable to a two-ventricle repair. The most severe form of HLHS has aortic atresia with mitral valve atresia and a very small left ventricle (**Figure 1B**). There are several other kinds depending on the severity of narrowing of different structures. Individuals with HLHS are ductal-dependent because there is inadequate systemic outflow through the usual pathway.

Student: That makes sense. So given that there is little to no forward flow through the aorta, a fetus with HLHS is adequately perfused *in utero* by backwards flow across the

patent ductus arteriosus to supply the head, neck, and coronary arteries with blood **(see Figure 2 for an example of fetal blood flow in HLHS).**

Fellow: Yes. Can you think of why there might be an acute decompensation postnatally?

Student: Patients with HLHS are ductus-dependent, meaning that they are dependent on the ductus arteriosus being open or patent to survive.[2] After birth the ductus arteriosus begins to naturally close in the first few days of life resulting in a significant reduction in perfusion of the systemic circulation and coronary arteries, which can lead to death if unrecognized and untreated.

Fellow: Correct. How does oxygenated blood flow in a newborn with HLHS?

Student: The ductus arteriosus must remain patent and there must be adequate left-to-right shunting at the atrial level for survival. Oxygenated blood flows from the left atrium via a left-to-right atrial shunt (patent foramen ovale), which then mixes with venous blood in the right atrium.
The mixed blood flows from the right atrium to the right ventricle and is pumped through the pulmonary artery. Blood flows from the pulmonary artery to the branch pulmonary arteries and with a patent ductus arteriosus blood can also flow from the pulmonary artery across the ductus arteriosus to the aorta, allowing perfusion of the systemic circulation. Blood will go from the patent ductus arteriosus up to the head, neck and coronaries, as well as to the descending aorta to supply the body **(Figure 2)**.

Fellow: Yes. The right ventricle thus supplies the pulmonary, coronary, and systemic circulations.
HLHS is the most frequent cause of heart failure in neonates and is implicated in 23% of cardiac deaths in the first week of life and 15% of cardiac deaths in the first month of life.[4]

If these patients are not detected by fetal echocardiography, they typically present within hours to days of birth when the ductus arteriosus begins to close. They will present with acute deterioration, starting with pallor, tachycardia, and weak pulses, and progressing to peripheral edema, pulmonary edema, cyanosis, hypotension, and hepatomegaly. If this continues without intervention cardiogenic shock with oliguria or anuria and metabolic acidosis will occur followed by death. Luckily Olivia has not yet reached that stage.

Student: Is Olivia likely to have other cardiac or extracardiac anomalies?

Fellow: Good question. 25% of individuals with HLHS have other cardiovascular anomalies, including coarctation of the aorta, coronary anomalies, ventricular septal defect, and anomalies of the pulmonary veins or tricuspid valve.[2]

Extracardiac anomalies and genetic syndromes are identified in 15-30% of HLHS patients. These extracardiac anomalies are predominantly related to the central nervous system (e.g. agenesis of the corpus callosum, holoprosencephaly). The gastrointestinal system can also be involved (e.g. diaphragmatic hernias, duodenal atresia, intestinal malrotation). Syndromes and chromosomal anomalies associated with HLHS include Noonan syndrome, CHARGE syndrome, Turner syndrome, and Trisomies 13, 18, and 21.[4]

Can you walk through the physical exam findings that the GP presented to us over the phone? Let's try to understand it together.

Student: On exam, Olivia was tachypneic, diaphoretic, and cyanotic. She was lethargic but rousable. She had marked increased work of breathing, with nasal flaring, and subcostal and suprasternal retractions. Her lips were dusky and there was distension of her neck veins. Her extremities were pale and cool. Upper-extremity and lower-extremity pulses were +1 and symmetric in rate, rhythm, and volume in upper and lower limbs bilaterally. On auscultation of her lungs, breath sounds were decreased bilaterally to the bases with inspiratory and expiratory crackles at the bases. Inspection of her chest revealed a hyperdynamic precordium. On auscultation, Olivia was tachycardic, with a single S2 heart sound and S3 gallop. There were no murmurs. Her abdominal exam was significant for hepatomegaly, with the liver edge palpable 4 cm below the costal margin.[2,4]

Fellow: The single S2 heart sound heard is due to absence of the aortic valve component. The S3 heart sound is not always auscultated, but it can be heard in the setting of ventricular dysfunction. It is uncommon to hear murmurs in HLHS. Hepatomegaly is common, and predominantly in infants with a later presentation.[4] The cyanosis is due to venous admixture. Unlike coarctation of the aorta, the pulses in HLHS are diffusely weak in both the upper and lower extremities.

Given her presentation, what do you think the relative ratio of pulmonary to systemic blood flow was when she arrived at the ER in her home community?

Student: High. She had more pulmonary blood flow than systemic blood flow.

Fellow: That's right. Right now with her PDA open the blood flow to her pulmonary and systemic circulation is nicely balanced with an O_2 saturation of 80%. Let's review Olivia's chest x-ray and ECG. What stands out to you in her chest x-ray?

Student: There is increased vascular markings.

Fellow: Right. It's worth mentioning that if we were to do a chest x-ray right after birth, the chest x-ray may actually appear normal. The findings that you mentioned generally

appear after the first 24 h of life, due to decreased pulmonary vascular resistance and the resulting increased pulmonary blood flow. If this patient had an intact or restrictive intra-atrial communication, we would see findings of pulmonary edema quite early on.[5]

Can you walk me through her ECG?

Student: Olivia is in sinus rhythm at a rate of 180 bpm. She has right axis deviation with a tall R wave in V1 and a deep S wave in V6.

Fellow: Correct. There are very little left-sided forces on her ECG which goes with left ventricular hypoplasia. Patients with HLHS are also normally in sinus rhythm, as you mentioned, as conduction disturbances are not common.[5]

Student: She's cyanotic. Why aren't we giving her oxygen?

Fellow: The goal is to have a balanced circulation – meaning 1:1 pulmonary and systemic blood flow. An oxygen saturation of 70-80% is a clue that we have achieved this. Too much pulmonary blood flow, or Qp, would mean too little systemic blood flow, or Qs. This would result in high oxygen saturation, but at the expense of a reduced systemic perfusion leading to poor pulses or reduced urine output, for example.

Student: Oh I see – and because oxygen is a vasodilator, and we don't want to decrease the pulmonary vascular resistance.

What's next for Oliva?

Fellow: HLHS has a very poor prognosis if not surgically palliated. If untreated, 80% of children will die in the first week of life. However, surgery is not without its risks, and families must be counseled regarding their options, including stopping treatment and compassionate care, surgical palliative procedures, and heart transplant, if available.[2] We will find out what Olivia's family and care team decide to do in the morning.

* * *

The next morning in clinic you meet up with the pediatric cardiology fellow, who updates you on Olivia.

Fellow: Good morning! I was speaking with the accepting pediatric cardiologist here at the children's hospital and I'd love to give you an update on Olivia. Olivia was diagnosed with HLHS. She was found to have left ventricular hypoplasia, with mitral atresia and aortic valve atresia **(Figure 1B).**[5]

Student: Is it typical that we would not have known about this condition prior to birth?

Fellow: Today many cases of HLHS are picked up during the routine 20-week detailed anatomical ultrasound,[4] and it can be detected as early as 16 weeks.[5] This early diagnosis allows for parental counselling and potential intervention, if necessary. HLHS is most easily diagnosed when the left ventricular chamber is found to be small and muscle-bound. Most cases of HLHS are thought to be progressive and dynamic throughout gestation, due to altered left ventricular outflow or inflow.[6-8] Fetal echocardiography also helps to identify those with a severely restrictive or intact atrial septum prior to birth, as their outcomes can be particularly poor and they may also benefit from immediate intervention.[4]

In Olivia's case, her mother was unable to attend her 20-week detailed anatomical ultrasound because of the remote location of the community she lives in and difficulty acquiring transportation to the nearest town that performs obstetrical ultrasounds. It is not uncommon in situations of newborns with duct dependent circulations, like Olivia, that they can examine relatively normally at birth, and only become symptomatic hours to days later, when the ductus begins to close.

Student: What is the role of interventional catheterization in HLHS?

Fellow: Interventional catheterization is useful in the setting of HLHS if there is a restrictive atrial shunt (a barely patent foramen ovale or a small atrial septal defect) as an atrial balloon septostomy can be performed to avoid further pulmonary congestion or edema. It can also be a useful diagnostic test in certain types of HLHS such as mitral stenosis and aortic atresia which can be associated with abnormal coronary connections.

In Olivia's case, this was not necessary. No further diagnostic information was needed from a cath and her atrial communication was adequate. The cardiac intensive care team was able to provide adequate stabilization and Olivia's mother met with the cardiology team to discuss Olivia's options. Olivia's mother elected to pursue surgical palliation. Do you know what procedure they elected to do?

Fortunately after your encounter with Olivia the day prior you had done some quick reading on treatment options for HLHS and had an answer prepared for your fellow.

Student: I was reading that there are two types of initial Stage I palliative surgeries - the Norwood Sano and the BT shunt (**Figure 3A-B**). What did they choose to do?

Fellow: They have booked a Norwood procedure with a Sano shunt to be done on day 6 of life. **(Figure 3B).**[2] Do you know what the purpose of this procedure is?

Student: The first stage must accomplish 3 things – unrestricted mixing, unobstructed systemic outflow, and restricted supply of pulmonary blood flow. A Norwood procedure with a Sano or modified BT shunt accomplishes this. The atrial septum is resected to

allow for unrestrictive mixing of the venous return. A “neo-aorta” (new aorta) is created by anastomosing the hypoplastic aorta with the pulmonary artery and widening the aortic arch. This supplies the systemic circulation with blood. Lastly, it establishes restricted pulmonary perfusion via shunting blood from the right ventricle to pulmonary artery (a Sano shunt) or by an aortopulmonary shunt (a modified BT shunt) connecting the right subclavian artery to the ipsilateral (or same-sided) pulmonary artery.[2]

Fellow: Exactly. Following her Stage I surgical palliation, the interim stage is focused on supporting organ function and somatic growth. Management during this time focuses on pharmacologic therapy optimizing efficiency of circulation, identifying concerning pathophysiology, and supporting growth.[4] Patients will be monitored for cyanosis (SpO_2 <75%), and poor weight gain.[1]

We should probably get moving with our clinic for today, but maybe you’ll get a chance to see Olivia when you’re on your pediatric cardiac surgery rotation. Didn’t you mention you would be doing that in a few months?

* * *

Four months later you are on your surgical subspecialty rotation, which happens to be pediatric cardiovascular surgery. During your rotation you see Olivia, now 5 months old, accompanied by her mother for her Stage II surgery (Bidirectional Glenn). You are delighted to see that Olivia is interactive and smiling in her mother’s arms. You are also pleased to hear that Olivia and her mother have been well supported by the children’s hospital’s heart center, as well as by her pediatrician in her local community. They received a weekly phone call from a cardiac nurse, as well as had regular appointments with their pediatrician. Your cardiac surgery attending is surprised, but happy to hear of your knowledge of Olivia and her case.

Preceptor: As you can see, Olivia is 5 months old, which is a typical age for Stage II surgical palliation. We typically do this procedure anytime between 4 and 6 months, or in select cases earlier than 4 months if interstage mortality is deemed high.[4] Olivia’s pre-operative catheterization is reassuring and her other testing has been normal. I’m presuming that you’ve read up on the surgery that she is scheduled for?

Student: Yes. We’re planning to do a bidirectional Glenn, which anastomoses the superior vena cava to the right pulmonary artery. The venous blood from the upper body can flow passively into the lungs **(Figure 3C)**. The Sano or BT shunt is removed, as it is no longer necessary.

You scrub in and assist on Olivia’s bidirectional Glenn procedure, which goes successfully. Olivia is discharged home with appropriate pediatric cardiology follow up.

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Almost 4 years later you're a 3rd year pediatrics resident on your cardiology rotation. In clinic you see 4-year-old Olivia, here for her pre-Fontan assessment. You are delighted to see Olivia again, who has grown into an energetic, interactive little girl. You complete Olivia's history and physical exam, and proceed to review with the attending cardiologist.

Preceptor: I understand that you have a longstanding history with Olivia's case. That's great that you have been able to achieve such continuity of care throughout your training! Tell me, how did they determine the timing for her final palliative surgical procedure?

Resident: Given that Olivia received Stage II palliation, the timing of Stage III, her Fontan procedure, is not critical. Usually it is electively performed around 3 to 4 years of age. Olivia has been progressing and developing well since her Stage II procedure. The timing of the procedure is more based on the progression of her symptoms.

Preceptor: Can you explain to me the basics of what a Fontan surgery achieves?

Resident: The surgical goal of this procedure is to completely separate blue deoxygenated blood and red oxygenated blood. In this way, the blue deoxygenated blood from the upper half of the body will flow through the Glenn at the top, and the blue deoxygenated blood from the lower half of the body will flow through the extracardiac Fontan. This is accomplished surgically by routing blood from the inferior vena cava to the pulmonary arteries.[4]

Preceptor: Yes, that's the general idea. There are many different kinds of Fontan procedures (**Figure 3D-F**), but the extracardiac Fontan (**Figure 3F**) is now the most common Fontan procedure. During this procedure a prosthetic conduit is placed between the pulmonary arteries and the inferior vena cava, which is either fenestrated or nonfenestrated.[4] The purpose of fenestration is to allow for right-to-left shunting, improving ventricular preload and cardiac output and decreasing central venous pressure. This, however, is at the expense of cyanosis. Fenestration has resulted in shorter hospital stays and excellent survival in select patients.[9]

Resident: What kind of follow up will Olivia have and who will provide this? Because you've been following Olivia for a while, what resources and supports are you aware of Olivia and her family being connected to?

Preceptor: Her cardiologist and pediatrician will be her main team that are looking after her follow-up and screening for any post-Fontan complications. Congenital heart disease is associated with a number of neurodevelopmental concerns, as well as other potential complications that require routine screening and monitoring. She will be

followed annually by cardiology, and more frequently by her general pediatrician as she grows and develops.

The pediatric cardiologist and pediatric cardiac surgeon examine Olivia and review her most recent echocardiogram, cardiac catheterization, and ECG. They are pleased with her current clinical status and book a date for her Stage III palliation surgery, a fenestrated extracardiac conduit Fontan after discussing her case at the combined cardiology and cardiac surgery case conference. Olivia undergoes a successful operation and has regular pediatric cardiology follow-up.

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There are many short-term and long-term complications and sequelae associated with the Fontan circulation. To learn more about these and see how Olivia and Jason are doing in late adolescence, please refer to the third and final episode of this PedsCases podcast series.

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Recommended resources for learners

Allen HD, Driscoll DJ, Shaddy RE, Feltes TF. Moss and Adam's Heart Disease in Infants, Children, and Adolescents. Philadelphia: Lippincott Williams & Wilkins; 2013.

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Figures

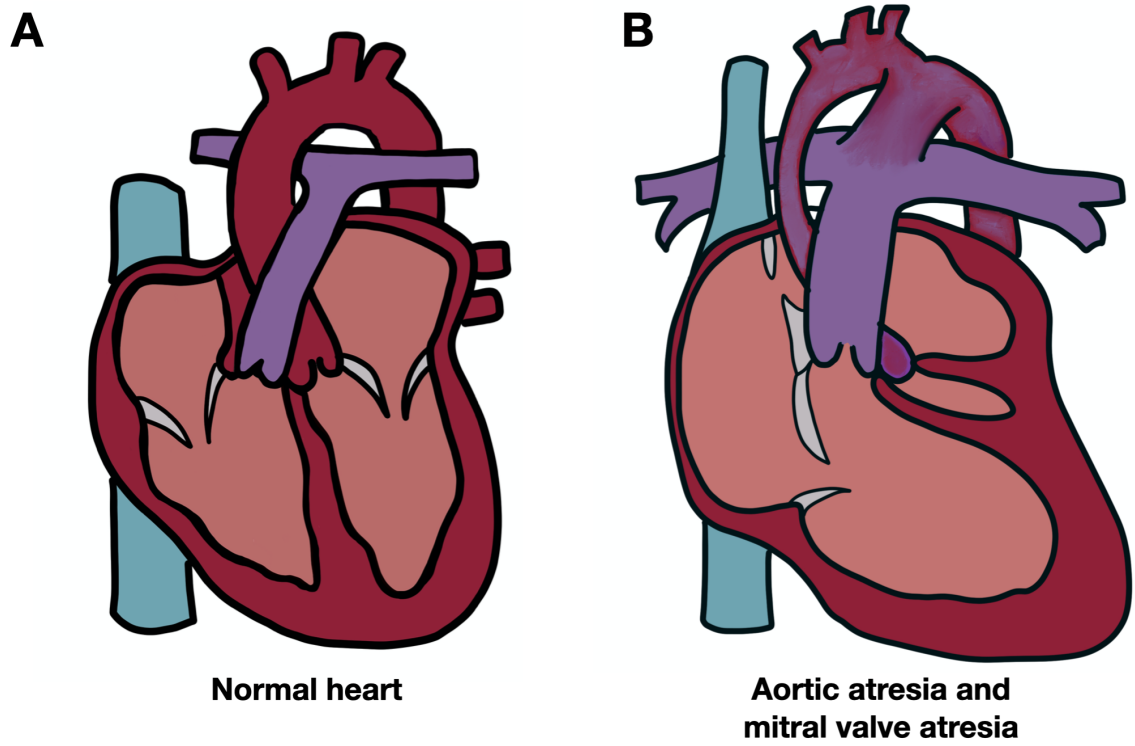

Figure 1: Normal cardiac anatomy compared to the anatomy of the most severe form of hypoplastic left heart syndrome – aortic atresia and mitral valve atresia. Figure by S. Laguë.

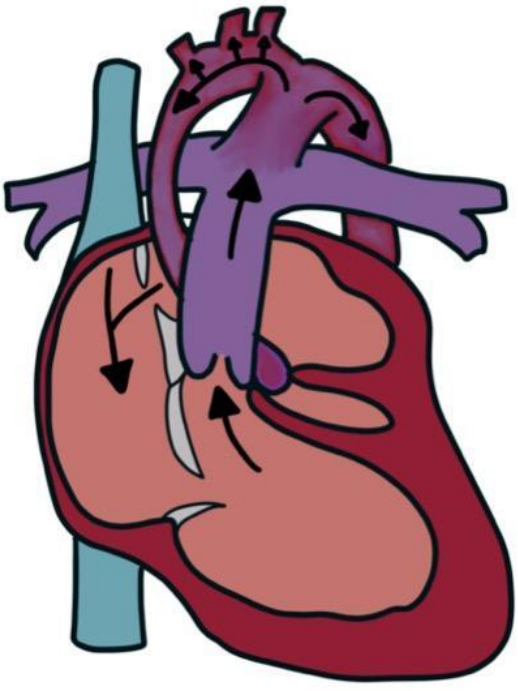

Figure 2: Direction of fetal blood flow in hypoplastic left heart syndrome. Figure by S. Laguë.

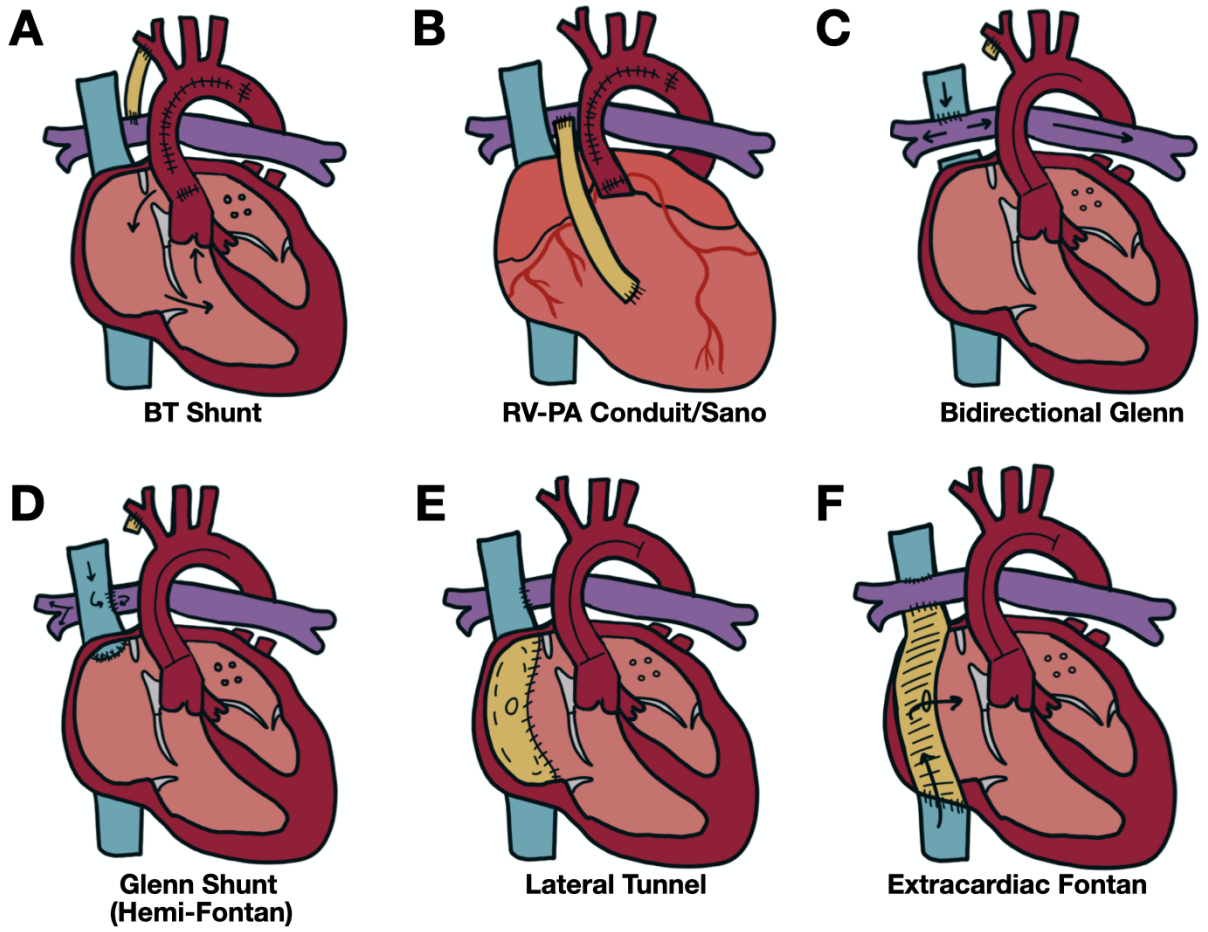

Figure 3: Surgical palliation repairs available for anatomically and functionally single ventricles. These include the (A) BT (Blalock-Tasussig) Shunt, the most common primary shunt procedure; the (B) right-ventricle to pulmonary artery (RV-PA) conduit/Sano; the (c) Bidirectional Glenn), the most common second stage procedure, and its alternative, the (D) Glenn shunt or hemi-Fontan; and two forms of third stage procedures, the (E) lateral tunnel and (F) extracardiac Fontan (with or without fenestration). Figure by S. Laguë.

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