Creating a Systematic Framework Approach to Congenital Heart Disease Comprehension and Management – A Primer for the Cardiac Intensive Care Unit Provider

AUTHORS

Richard P. Lion, DO, MPH, FAAP *Division of Pediatric Critical Care, Loma Linda University.*

Saul Flores, MD, FAAP, FACC *Section of Critical Care and Cardiology, Texas Children's Hospital*

Rohit S. Loomba, MD *Division of Pediatric Cardiac Critical Care, Advocate Children's Hospital, Chicago Medical School*

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Background and Introduction

The pediatric cardiac intensive care unit (PCICU) is a setting where cardiac morphology, function, and physiology are intimately intertwined. Congenital anatomic malformations of the heart perturb circulatory physiology in a manner not encountered elsewhere, creating high risk of morbidity and mortality. Thus, it is in the PCICU that some of the most unique and critically ill patients receive care [1, 2].

With the continued growth of complex congenital heart malformations able to be palliated or repaired, the number of clinical scenarios that may be encountered in the CICU is difficult to quantify [1, 3, 4]. Add the presence of extracardiac anomalies or pathologies and this number can increase exponentially. An estimated 1.35 million patients are born with Congenital Heart Disease (CHD) annually, with survival for even the most complex lesions expected to be ~ 90% in developed countries, shifting focus towards improved neurodevelopmental and psychosocial outcomes and resource utilization [3-9].

With improved survival comes an increased burden for CHD care provision both inside and outside the CICU [10, 11]. Current providers and learners (physician and nursing students, residents and fellows) alike are responsible for understanding the individual medical and surgical treatment options for each CHD lesion. Thus, these patients, while no less complex, are being increasingly thrust into the care of the unfamiliar [12, 13].

While time and experience are requisite precursors for a certain level of mastery and knowledge attainment, even in the authors' own experiences with advanced cardiac intensive care training, we felt there lacked a systematic approach to CHD comprehension. Therefore, we sought to develop a thoughtful and logical approach to clinical management in the CICU to optimize provider ability and patient outcome.

The goal of this manuscript is hypothesis-driven and proof-of-concept in nature, an attempt at creating this "systematic framework approach to CHD management" or "physiologic primer" and offering it for consideration and commentary. The intended audience includes providers, educators and learners of congenital heart disease medicine with a shared goal for improving care through accessible knowledge and education.

CHD results from failure of expected embryologic maturation, segmentation and physiologic transition of the fetal bulbus cordis into the chambered, segmented neonatal heart[14, 15]. What results is the inability to provide separate pathways for de-oxygenated and oxygenated blood to effectively circulate, due to portions or in some cases all of these pathways being underdeveloped, resulting in ineffective mixing of blood and oxygen exchange.

The "sequential segmental approach" has greatly aided in providing a systematic framework for the abnormal *anatomic* development of CHD lesions [16, 17]. By limiting the variability to discrete segments such as atrial, valvular, ventricular and great arterial relationships, the learner can process every future lesion encountered through this approach to successfully identify CHD anatomy [18]. We hope to accomplish the same with the *physiologic* framework that follows: The Seven Physiologic Principles of Congenital Heart Disease, The Six Physiologic States of Congenital Heart Disease, and The Seven Questions to Answer for Every Congenital Heart Disease Lesion.

[TABLE 1]

The Seven Physiologic Principles of Congenital Heart Disease

1. Blood Follows the Path of Least Resistance
2. Lack of Blood Flow causes Lack of Heart Growth
3. Left Sided Obstructions cause Left Sided Underdevelopment
4. Right Sided Obstructions cause Right Sided Underdevelopment
5. "Critical" Lesions are Both Ductal and Intracardiac Mixing Dependent
6. "Critical" Left and Right Sided Obstructions Do Not Occur Together
7. Being Blue is Better than Being Gray

The seven physiologic principles of CHD build upon one another in a similar fashion to the sequential segmental approach to anatomy, and are given further elucidation below, utilizing "Critical" Pulmonary Stenosis (PS) and "Critical" Coarctation of the Aorta (CoA) as relative examples [TABLE 1].

Blood Follows the Path of Least Resistance

Blood flow is determined by the relative resistance of competing chambers and vascular beds both in the fetal and post-natal circulations [19]. In the structurally normal heart, fetal circulation demonstrates this with ductal dependent blood flow providing fetal oxygenation from mother's placenta, bypassing fetal lungs due to their elevated vascular resistance [19]. Only after birth, with spontaneous respiration increasing lung volume and lowering pulmonary vascular resistance, significant pulmonary blood flow begins.

In the setting of right or left outflow tract obstructive lesions, blood flow to the obstructed vascular bed continues to be dependent on a patent ductus post-natally [20, 21].

Lack of Blood Flow causes a lack of Heart Growth

In utero, the shear stress on cardiac chambers from contractile blood flow provides impetus for structural growth and maturation [14, 15]. Lack of in-utero blood flow to either the right or left-sided heart structures contributes to their underdevelopment, whether that is due to upstream obstruction to blood inflow-such as obstructed total anomalous pulmonary venous return decreasing blood flow into the left side of the heart, or tricuspid atresia decreasing blood flow into

the right side of the heart-or downstream obstruction to blood outflow such as "Critical" PS or CoA. This has been referred to as the "no flow, no grow" hypothesis [22, 23].

Building on the earlier concepts of blood flow being required for heart growth and blood following the path of least resistance, we wish to frame obstructive lesions for the learner/provider as a focus on the "side" of the heart that is expected to have problems related to underdevelopment, in order to guide diagnostic evaluation and management considerations.

Left Sided Obstructions cause Left Sided Underdevelopment

"Critical" CoA is a potential nidus for the spectrum of lesions encompassed by the terminology "Borderline Left Ventricle" (varied underdevelopment of left sided arterial, valvular and ventricular structures) and the more severe "Hypoplastic Left Heart Syndrome" (HLHS); yet these patients usually have well developed right atrial and ventricular chambers* [21–25]. Therefore, initial diagnostic focus should be on relative development of the left ventricular outflow tract (LVOT), and management be on the degree of obstruction to systemic blood flow and need for ductal patency. Surgical considerations include the ability of the left ventricle and atrium to support pulmonary venous return and systemic blood flow [21, 23, 25, 26].

Right Sided Obstructions cause Right Sided Underdevelopment

Building on the earlier concepts of blood flow being required for heart growth and blood following the path of least resistance, we wish to frame obstructive lesions for the learner/provider as a focus on the "side" of the heart that is expected to have problems related to underdevelopment, in order to guide diagnostic evaluation and management considerations.

"Critical" PS, or more severely, complete pulmonary atresia contributes to underdevelopment of the right ventricular outflow tract (RVOT) [20, 27]. The contralateral "side" is usually a well-developed left atrium and ventricle*. Here, initial diagnosis of RVOT development and need for ductal patency for pulmonary blood flow are paramount, while surgical considerations of the ability of the right heart to support systemic venous return and pulmonary blood flow are warranted [20].

**The authors purposely chose "well developed", to describe an atrium and ventricle capable of receiving and providing it's intended cardiac output. Per principle #5, "complete anatomic development" should not be expected, rather, the converse, a maintained source of intracardiac mixing and communication.*

"Critical" Lesions are Both Ductal and Intracardiac Mixing Dependent

The term "critical" equates ductal dependence for blood flow to the obstructed vascular bed [20, 21]. However, it is of equal importance that the provider understands that ductal dependent blood flow is bypassing an entire vascular bed usually contributing to oxygen delivery, thus relying on intracardiac mixing. To again build on the prior principles with our examples:

"Critical" PS should now be understood to require ductal patency for pulmonary blood flow due to severity of RVOT obstruction. Additionally, the "right side" needs evaluation for signs of underdevelopment due to lack of in-utero blood flow. In order to provide the pulmonary bed with de-oxygenated blood, systemic venous return must reach the left ventricle to be ejected into the aorta and PDA, best accomplished at the atrial level [20, 28, 29]. The converse, of course, being true for "Critical" CoA where ductal dependent systemic blood flow is required and oxygenated blood returning to the left atrium must reach the right ventricle to be ejected into the PA and PDA [21, 28, 29].

Perhaps the best elucidation of this principle is in the pre-operative physiology and management of dextro-transposition of the great arteries. These patients require ductal patency specifically to provide deoxygenated blood from the RV and Aorta to the PA and lungs [29-31]. Additionally, a source of intracardiac mixing must be identified or urgently created via balloon atrial septostomy to provide adequately mixed blood to be delivered to both vascular beds until definitive surgical correction [31].

"Critical" Left and Right Sided Obstructions Do Not Occur Together

Building on the above, and again to focus the efforts of the provider on pertinent principles of CHD recognition and management, a clinical scenario where severely or "critically" obstructed blood flow to both the pulmonary and systemic vascular beds is unlikely to be encountered [29]. Milder degrees of obstruction with well-developed bi-ventricular anatomy are encountered clinically, but unlikely to cause significant obstruction, necessitate ductal dependence or warranting the same physiologic considerations as the "critical" lesions described.

Being "Blue" is Better than Being "Gray"

One of the greatest successes of CHD management and cardiac intensive care has been our ability to palliate patients along the single ventricle pathway [32]. We have and continue to invest immense time and resources to provide oxygen saturations

of 75-85% and intend for children to develop for years with this physiology until the Fontan operation [28, 33]. With understanding of our body's inherent ability to adapt its oxygen carrying capacity in the form of cardiac output adaptations of the single ventricle and up-regulation of hematocrit production; as well as the unique physiologic challenges of providing balanced Qp:Qs within the single ventricle physiology, the importance of this principle is illustrated [28, 33]. Not only is this oxygen saturation adequate for somatic and neurodevelopment in early childhood, but the risks associated with attempting to enhance cardiac output or oxygen delivery to "normal" must be understood [28, 33, 34].

[TABLE 2]

The Physiologic and Saturation Goals of Congenital Heart Disease

Biventricular Physiology/Circulation	**Aortic SaO2 > Pulmonary Artery SaO2** *Systemic Saturation Goal: > 93%*
Limited Pulmonary Blood Flow	*Saturation Goal: > 93%*
Limited Systemic Blood Flow	*Saturation Goal: > 93%*
Single Ventricle Physiology/Circulation *Parallel Circulation (Pre and Post-Stage I)*	**Aortic SaO2 = Pulmonary Artery SaO2** *Saturation Goal: 75–85%*
Stage II Circulation	*Saturation Goal: 75–85%*
Stage III Circulation	*Saturation Goal: > 93%*
Transposition Physiology/Circulation	**Pulmonary Artery SaO2 > Aortic SaO2** *Saturation Goal Pre-Operatively: 75–85%* *Saturation Goal Post-Operatively: > 93%*

Despite seemingly endless anatomic types and subtypes of CHD, we offer a framework for the physiologic and three physiologic and saturation goals of congenital heart disease [TABLE 2]. Lesions such as HLHS are always associated with single ventricle physiology (SVP), while the Double Outlet Right Ventricle (DORV) physiology can be biventricular, single ventricle or transposition in nature depending anatomic variant [35]. While anatomy does not equal physiology, as is the case with DORV, it does dictate *physiologic potential*. Anatomic and physiologic behavior pre-operatively guides management and surgical-decision making, which will be given further consideration in the following section [TABLE 3].

Biventricular Physiology

The "normal" physiologic state of cardiac output, defined by the Aortic SaO2 being greater than Pulmonary SaO2. This can be achieved for those congenital heart disease lesions that have two well developed atria and ventricles and can be provided separate sources of venous return and arterial output through native or surgically placed structures [36, 37]. Post-operatively, the circulation is expected to be in-series with systemic saturation goals usually > 93%.

Single Ventricle Physiology

The physiologic goal of cardiac output for those congenital heart lesions that will be dependent on intra-cardiac mixing and shared cardiac output due to lack of development of both atria and ventricles [33]. Pre-operatively, due to the parallel circulation associated with intra-cardiac mixing dependence, Aortic SaO2 equals Pulmonary SaO2, with the ratio of systemic to pulmonary vascular resistance dictating the amount of systemic and pulmonary blood flow. Understand that the expectation of equal aortic and pulmonary artery saturation is only maintained until the time of Stage II or III circulation when pulmonary blood flow/venous return is directed away from the heart. Post-operatively, due to limitation of effective pulmonary and systemic blood flow and continued intra-cardiac mixing, saturation goals are usually 75–85% for the post-Norwood and Glenn patient [38]. At the time of the Fontan, all systemic venous return is directed to the pulmonary arteries, allowing for saturation goals to approach > 90% [39].

Transposition Physiology

The physiologic state of dextro-transposition of the great arteries prior to surgical correction. Due to this unique physiologic state, ductal patency and intracardiac mixing are required for adequate pulmonary and systemic blood flow [30]. The role of the ductus arteriosus in this physiologic setting is unique, due to pre-operative Pulmonary SaO2 being higher than Aortic SaO2. The lower saturation aortic blood can only reach the pulmonary arterial bed via the patent ductus until time of surgical correction, when systemic saturation goals become > 93%.

[TABLE 3]

The Seven Questions To Answer For Every Congenital Heart Disease Lesion

1. What is the anatomy?
2. What is the physiology?
3. How does blood get to the heart?
4. How does blood get to the body?
5. How does blood get to the lungs?
6. What are the medical options?
7. What are the surgical options?

Successful CHD management requires understanding of the interplay between anatomy and physiology pre-operatively, understanding of the surgical procedure necessary for palliation or repair, and the subsequent changes in anatomy and physiology occurring post-operatively, which can appear daunting to the unfamiliar. We can now incorporate the physiologic principles and goals of CHD into a framework for management in the form of these seven questions [TABLE 3].

What is the Anatomy?

Utilizing existing echocardiographic or catheterization data, the provider is encouraged to recognize any malformations, especially those resulting in remnant embryologic structures (Patent Ductus Arteriosus, Atrial Septal defect, Truncus Arteriosus, Bulboventricular Foramen). In the setting of "Critical" obstructive lesions like the examples provided earlier, any limitation of ductal patency or intracardiac mixing warrants immediate attention.

What is the Physiology?

Understanding the pre-operative physiology is of equal importance to the understanding of pre-operative anatomy, as well as the physiologic potential of the malformation. For those CHD malformations with pre-operative biventricular or transposition physiology, is it expected that the post-operative potential for biventricular physiology exists? For those CHD malformations with pre-operative single ventricle physiology, does the lesion have the anatomic or physiologic potential for post-operative biventricular or single ventricle physiology and circulations? [36, 37]

How does Blood get to the Heart?

Early recognition of any limitation to systemic or pulmonary venous return may warrant immediate surgical consideration, especially in the setting of obstructed total anomalous pulmonary venous return. Heterotaxy lesions, especially the left atrial isomerism variant, often have interruption of usual IVC return with continuation via the retained azygous system [40].

How does Blood get to the Body?

Recognize any systemic outflow obstruction warranting ductal patency and intracardiac mixing dependence prior to surgical intervention [21].

How does Blood get to the Lungs?

Recognize any pulmonary outflow obstruction warranting ductal patency and intracardiac mixing dependence prior to surgical intervention [20].

What are the Medical Options?

Certain CHD lesions themselves are indications for surgery, with medical management aimed at initial resuscitation and stabilization of end organ perfusion in anticipation of surgery, while others can benefit from medical heart failure therapy in an effort to safely delay surgery until outside the neonatal period. Despite the same armamentarium of critical care therapies available (volume resuscitation, supplemental oxygen, positive pressure ventilation, vasoactive support) the provider must understand what effect these therapies have on CHD physiology, especially that of the single ventricle and transposition patient, as compared to the intensive care patient with normal cardiac anatomy and physiology [30, 33, 41].

What are the Surgical Options?

When considering patients for surgical referral, we offer the following (admittedly non-straightforward) questions for the provider to consider for both their own edification and to enhance shared understanding of each patient's management goals.

- *Does the anatomy have biventricular or single ventricle physiologic potential?*
  As described above, anatomy dictates physiologic potential. Are there two well developed atria to receive venous return and two well developed ventricles to provide cardiac output, or would the patient be a better candidate for single ventricle palliation pathway? [25, 37]

- *How can we provide unobstructed systemic and pulmonary blood flow?*
  Are there two well developed great arteries, or will the patient require surgical creation of a pulmonary or systemic outflow tract depending on the location and severity of obstruction? [20, 21].

- *Is the surgery considered palliative or reparative?*
  Single ventricle palliation is named appropriately so, as it does not repair the heart disease back to usually biventricular anatomy and physiology. It is truly palliative, an attempt to lessen the severity of the disease, and should not be considered or construed to be curative of the underlying condition.

Case-Based Discussion: Double Outlet Right Ventricle with Mitral Atresia, Pulmonary Stenosis

What is the anatomy?

As the above has demonstrated, it is not ample for one to simply know that a patient has double outlet right ventricle (DORV). A much more in-depth understanding is required to understand which physiology that each individual DORV anatomy is dictating, given the potential to display biventricular, single ventricle or transposition physiology [35].

Recall that 16 distinct variants of DORV exist based on the relationship of the great arteries and position and location of the ventricular septal defect (VSD) [35].

What is the physiology?

Once the anatomy is clear one can begin to create a sense of what physiology would be expected in the patient. Expounding upon the three physiologic states presented above [TABLE 2], the following pathophysiologic categorizations have been frequently described.

- *Biventricular circulation with systolic or diastolic dysfunction*
- *biventricular circulation with right-sided obstruction*
- *biventricular circulation with left-sided obstruction*
- *biventricular circulation with left to right shunt*
- *biventricular circulation with right to left shunt*
- *biventricular circulation with systemic to pulmonary shunt*
- *Single Ventricle Physiology with Norwood Circulation*

- *Single Ventricle Physiology with Glenn Circulation*
- *Single Ventricle Physiology with Fontan Circulation*
- *Transposition physiology*

Using such a system of categorizing physiologies allows for quick description of patients when communicating with others in the CICU and also while trying to understand a patient's physiology for oneself. While each physiology will have some generally constant principles, each individual patient's hemodynamics will need to be superimposed to completely understand the physiology.

How does blood get to the heart, the lungs, and the body?

For instance, are both atrioventricular valves patient and of adequate size? Where is the interventricular communication and is it of adequate size? A sub-aortic interventricular communication portends a different physiology than a sub-pulmonary interventricular communication (biventricular physiology with left to right shunt versus single ventricle physiology parallel circulation). Are the outflow tracts obstructed, and if so which? Significant sub-pulmonary or pulmonary stenosis may limit pulmonary blood flow and right sided development. (Principle 3: Right sided obstruction causes right sided underdevelopment). Is this "critical PS" warranting ductal patency pre-operatively? (Principle 5: "Critical lesions are both ductal and intra-cardiac mixing dependent")

What are the medical options?

Consider the case of DORV with mitral atresia (MA) and non-critical pulmonary stenosis (PS). This anatomic and physiologic arrangement results in single ventricle physiology with parallel circulation. Now consider this patient presenting with relative hypoxia with saturations of 60% compared to the patient's expected saturation of 80%. Further investigation in this child should consist of cardiac function assessment, assessment of volume status, quantification of hemoglobin or monitoring of venous saturation directly or indirectly, and estimation of Qp:Qs balance.
Any deviations from the expected physiology should be identified and must be acted on. This requires frequent assessment and monitoring of patients. Whether this data comes from echocardiography, cardiac catheterization, advanced imaging, or hemodynamic monitoring it must be done in a timely manner with care taken to obtain the necessary data to help answer clinically relevant questions.

Continuing the management of our DORV/MA patient, imaging and laboratory assessment demonstrate no abnormalities except that the hemoglobin is 10 g/dl which is below baseline of 14 g/dl. Somatic near infrared spectroscopy (NIRS) is reading in the low 20s. You may now at this point identify the physiology at the moment to be that of venous desaturation secondary to relative anemia in the setting of parallel circulation. The intervention in this particular example becomes clear and you decide to transfuse the patient with packed red blood cells. At this point it becomes important to identify what may happen with the intervention. If your diagnosis is correct in this situation you would expect that an appropriate transfusion would lead to improved oxygen delivery, increased venous saturation (in this situation manifesting as improved renal near infrared spectroscopy), and increased arterial saturation. Repeat quantification of the hemoglobin should demonstrate appropriate increase. But what if the hemoglobin was to improve and the patient's arterial saturation and renal NIRS did not? Then you would undoubtedly have to be prepared to re-evaluate the current physiologic state.

Such explicit consideration of what change in physiology is expected with each intervention and how it will be monitored must be vocalized with all involved with the patient's care so there is a unified approach and understanding of how the intervention will be monitored. Herein lies a most crucial step in the process: continued monitoring and re-assessment during an intervention. To continue with our example, 15 ml/kg of packed red blood cells arrive in the unit and are administered over four hours to the patient. After an hour you note that the renal NIRS are improving as are the arterial saturations. You are now reassured that your diagnosis was correct and that your intervention was appropriate. If you did not note the expected changes you may decide to let more of the blood be administered before additional evaluation but you should at least reiterate what next steps are. What if there were minimal improvement in the patients' arterial saturation, renal NIRS and hemoglobin level after the blood transfusion is complete? Now you may decide to evaluate for sources of bleeding.

Such a method also enhances team communication as it allows for a framework by which to communicate pertinent information to the team in a way that allows for understanding of a patient's anatomy, physiology, current active issues, the planned intervention, expected results of the intervention, and how the results will be monitored. Returning to the clinical

example and applying this framework one could summarize the patient concisely as follows: "this is a young child with double outlet right ventricle with pulmonary stenosis and mitral atresia with single ventricle physiology and parallel circulation who presents with acute hypoxia and venous desaturation believed to be secondary to anemia. Will plan to transfuse packed red blood cells which should result in improvement in renal NIRS, arterial saturation, and hemoglobin. If these improvements aren't seen, or not to the expected degree, then would consider looking for a source of bleeding".

Having a systematic method of clinical management, although intuitive, does take conscious effort, particularly for those early in their CICU experience. Such a framework of clinical management should also help instill confidence in the team and the patient or their family as it concisely communicates the pertinent information and outlines expectations. Such a methodology can be applied to multiple active issues at once, a scenario often experienced in the CICU.

What are the surgical options?

Management for this patient should include counseling regarding the palliative nature of the single ventricle pathway, with medical management aimed at optimization pre-operatively for stage 1 repair. For more details and educational content regarding anatomic and physiologic subtypes of DORV, as well as the single ventricle palliation pathway, we encourage the reader to explore the references below in addition to the Heart University website.

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