Pathophysiology of Congenital Heart Disease in the Adult
Part III: Complex Congenital Heart Disease

Robert J. Sommer, MD; Ziyad M. Hijazi, MD, MPH; John F. Rhodes, MD

With the successes in cardiothoracic surgery and pediatric cardiology over the past 3 decades, for the first time, adults with congenital heart disease (CHD) outnumber their pediatric counterparts. As a result, adult patients with CHD are beginning to appear more frequently in the practices of adult cardiologists. The present series is designed to provide a review of the pathophysiology and natural history of common congenital heart problems that are now being seen by adult cardiologists. In the first 2 parts of the series, simple shunts and congenital obstructive lesions were reviewed. This final chapter will examine the physiology and natural history of and the indications for intervention in common complex congenital cardiac malformations seen in adult patients. These patients include those with single-ventricle physiology who are reaching adulthood in significant numbers for the first time, the early survivors of innovative surgical techniques developed a generation ago.

The combination of shunts, obstructive lesions, chamber hypoplasia, and abnormal arterial and venous connections that is seen in this group of patients creates some of the most interesting and complex changes in the normal physiology of the heart. Each patient must be considered individually, because small differences in septal defect size or pathway obstruction may have an enormous impact on the overall effectiveness of the circulation and on management of the patient. For the purposes of this article, only the most common types of complex CHD will be considered (those that are most likely to be seen in the adult cardiologist’s office). However, the principles of flow and resistance, as reviewed in the prior 2 portions of this series and as related below, are easily generalized to give the practicing physician insight into the physiological consequences of a myriad of rare cardiac malformations.

Adults with complex CHD can be divided into 2 groups: those who have not previously had an intervention and those who have. The former will present with new-onset symptoms in adulthood or may be identified as a result of a physical examination with a new physician, an abnormal ECG, or before they begin a new job. Children in the latter group who have had good outcomes from surgical interventions are frequently lost to follow-up during adolescence. They may return for care in early adulthood with ongoing or new symptoms or for clearance for employment, higher education, insurance, or sports. These patients are often unfamiliar with their diagnoses and their surgical history, have long since stopped taking medication, and have adapted to a lifestyle that fits their level of cardiac function.

Adults Presenting With No Prior Surgery
Like many patients with simple congenital lesions, some adults with complex CHD may reach adulthood without having had a prior intervention, or occasionally without even having had a diagnosis. These patients generally have remained undiagnosed because of the absence of significant clinical symptoms, although the lack of diagnosis may also result from the limited availability of medical care in some parts of the world.

Ebstein’s Anomaly of the Tricuspid Valve
Ebstein’s anomaly of the tricuspid valve (TV) is a well-described congenital malformation in which the septal leaflet of the TV is conjoined to the septal surface well below the valve annulus into the body of the right ventricle (RV; Figure 1). The other 2 leaflets of the valve elongate to coapt with the abnormal septal leaflet, displacing the resulting coaptation point into the RV outflow tract.

Pathophysiology
There are 2 significant hemodynamic outcomes of the malformation. First, coaptation is rarely adequate, so most patients have at least moderate TV regurgitation. Second, the effective RV chamber size is reduced (and the right atrial [RA] size increased) by a magnitude that corresponds to the displacement of the TV. The small size of the RV diminishes its filling capacity, which results in increased impedance to filling. RA filling pressures are elevated, exacerbated by the tricuspid regurgitation. In more severe cases, venous congestion may result. The frequent association of an atrial septal...
communication, either an atrial septal defect (ASD) or a patent foramen ovale (PFO), will allow right-to-left shunting with RA pressure elevation, particularly with exertion (when cardiac output is increased and the RV is asked to accept more volume).

Natural History
Clinical symptoms are highly variable and are related principally to the degree of TV displacement. With mild disease, the patient may be asymptomatic, and the diagnosis may be discovered incidentally during an echocardiogram performed for other reasons. The patient may present with a murmur of tricuspid regurgitation or with supraventricular tachycardia (accessory bypass tracts are a common association). With more severe valve displacement and an intact atrial septum, the patient may present with exercise intolerance. Although the small RV may be able to produce a normal resting output, it is preload limited, which limits its stroke volume. As demands increase on the “maxed out” RV, left ventricular (LV) preload requirements will not be met, which limits systemic cardiac output. Signs of systemic venous congestion may be present with exertion.

The more common presentation is that of a patient who also has an ASD or PFO. These patients may also present with exercise intolerance. However, with an atrial communication, when RV capacitance becomes inadequate and RA pressure rises with exertion, the patient will develop a right-to-left shunt at the atrial level. In contrast to the patient with an intact septum, when RV output cannot meet the preload requirements of the LV, the right-to-left shunt augments/normalsizes LV preload and output, at the expense of systemic arterial hypoxemia. In this population, even though resting oxygen saturation may be normal at rest, exercise intolerance is usually due to falling saturations, not to low cardiac output. This can easily be proven during exercise stress testing. With an atrial communication and right-to-left shunting, these patients may also present with paradoxical thrombotic embolization.

Indications for Intervention
The management of the patient with Ebstein’s anomaly depends entirely on the degree of symptoms. In asymptomatic patients, no intervention is required. In patients with arrhythmia who are otherwise symptom-free, medical management or radiofrequency ablation may be their only need. For patients who present with exercise-induced cyanosis who are normally or nearly normally oxygenated at rest, transcatheter closure of the PFO/ASD may be an excellent option.

We typically assess the physiological impact of PFO/ASD closure in the catheterization laboratory with temporary balloon occlusion of the septal communication, which eliminates the shunt to the left heart. We can measure the corresponding rise in RA pressure and the associated drop in cardiac output (Fick technique) as the right-to-left flow is eliminated. In patients with low resting filling pressures and normal or nearly normal arterial saturations at rest, these changes should be minimal, and closure of the defect may proceed. In patients in whom RA pressure exceeds 15 mm Hg with balloon occlusion, those in whom there is a significant jump in RA pressure from a low baseline pressure to >15 mm Hg with balloon occlusion, and those in whom there is a substantial fall in cardiac output with balloon occlusion, the atrial communication should likely be left open. The tradeoff of low cardiac output for full oxygen saturation is often not beneficial for the patient, because tissue oxygen delivery (the product of oxygen content and cardiac output) is usually less after elimination of the shunt, as has been demonstrated with a number of other congenital malformations.

In the unusual case of an adult patient presenting with a small RV volume, tricuspid regurgitation, and true right-sided heart failure symptoms, surgical reconstruction or replacement of the TV in the annular position is probably the best option. An alternative surgical approach, which has been used primarily in children, is the “11/2 ventricle repair,” in which a bidirectional Glenn shunt is performed (superior vena cava disconnected from the RA and anastomosed directly to the right pulmonary artery). This allows the blood returning from the upper body to drain directly to the lungs and back to the LV, whereas the small RV is unloaded and needs to handle only return from the inferior vena cava. As a rule, most patients with Ebstein’s anomaly and significant symptoms due to hypoplasia of the RV will have undergone prior surgery as children, receiving either restorative valve surgery or single-ventricle repairs.

L-Transposition of the Great Arteries (Physiologically “Corrected” Transposition)
L-transposition of the great arteries (L-TGA) is the result of abnormal ventricular looping of the developing fetal heart, in which the primitive ventricle moves to the right and the bulbous cordis moves to the left. Because these structures are the precursors of the LV and RV, respectively, the morpho-
logical RV and TV end up on the left side of the heart, receiving blood from the left atrium (LA) and pumping blood to the aorta, whereas the morphological LV and mitral valve receive inflow from the RA and deliver deoxygenated blood to the lungs (Figure 2). The aortic root, arising from the RV, is anterior and leftward of the pulmonary artery root (“L” transposed). The inverted atrioventricular (AV) connections, combined with the reversed ventriculoarterial connections, “correct” the flow pattern such that deoxygenated systemic venous blood flows to the lungs, and oxygenated pulmonary venous return (white arrow) is pumped to the aorta by the RV. Ao indicates aorta; MPA, main pulmonary artery.

Natural History
Because the initial physiology of isolated L-TGA is normal, children rarely have cardiac symptoms or even heart murmurs. It is the potential late failure of the RV and TV, which both face the higher-resistance systemic arterial circuit, that most frequently brings these patients to attention as young adults. In this group, progressive dilation of the RV, as the myocardium fails, typically leads to enlargement of the TV annulus and worsening of the tricuspid regurgitation. The volume load of the tricuspid regurgitation, in turn, worsens RV chamber dilation, which further stretches the tricuspid annulus. This progressive process has comparable physiological consequences to those of a patient with a failing LV who develops mitral regurgitation. Longitudinal studies have described outcomes in patients with and without surgical intervention.\textsuperscript{10,11}

The septum (and the conduction system tissue that runs through it) is reversed, such that depolarization of the septum occurs from right to left (morphologic LV to morphologic RV). This typically produces a qS pattern in the right sided precordial leads, and the absence of Q waves in the left precordial leads. Complete heart block is a frequent accompanying or presenting symptom in this population owing to the associated abnormal development of the conduction system.\textsuperscript{12} Other associations include an Ebstein-like displacement of the left-sided TV (common), which may contribute to TV dysfunction, and ventricular noncompaction (rare), which may contribute to ventricular dysfunction.\textsuperscript{13}

Indications for Intervention
Management of patients with isolated L-TGA is symptom-dependent. Most often, patients present with signs of congestive heart failure, and management may be attempted with the usual array of medications that would be considered in a patient with a failing LV and a regurgitant mitral valve (digoxin, diuretics, and afterload-reducing agents). There is limited evidence that these therapies are as effective in the L-TGA population. Care must be taken in patients with underlying A-V conduction issues when drugs such as β-blockers or calcium channel blockers are used. TV replacement therapy is reserved for those patients with severe tricuspid regurgitation who have well-preserved RV function.\textsuperscript{14}

For patients with symptomatic heart block, pacemakers may be placed transvenously, as in any other patient, although the ventricular lead will end up in the right-sided morphological LV. Cardiac resynchronization therapy has been used in small series for heart failure symptoms, with some apparent benefit in this population.\textsuperscript{15} Heart transplantation is a final common pathway for patients with severe heart failure symptoms. The unusual relationship between the aortic and pulmonary trunks is the unique complexity facing the transplant surgeon in fitting the new organ into the patient.

Unrepaired Tetralogy of Fallot
Tetralogy of Fallot is the most common complex cyanotic congenital heart lesion. It also has the longest surgical history and the most intensively studied outcomes and follow-up data of all congenital cardiac anomalies. Adult patients with unrepaired tetralogy of Fallot are extremely rare; however, in areas where patients have no access to health care, particularly in developing countries, some of these patients may survive to adulthood.

The 4 distinct components of the tetralogy, as described in 1888 by Fallot, include VSD, subpulmonary stenosis, overriding aorta, and RV hypertrophy (Figure 3). However, embryologically, the defect appears to be a single developmental error\textsuperscript{a} that involves the terminal portion of the spiral septum, which divides the primitive truncus arteriosus from the pulmonary artery. In tetralogy of Fallot, this muscle bundle is displaced rightward and anteriorly, which precludes
by guest on April 15, 2017 http://circ.ahajournals.org/ Downloaded from

The resistance of the pulmonary path is extremely variable
from 1 patient to the next. If the obstructive lesions are mild,
the net resistance to pulmonary flow will be low compared
with the resistance to systemic arterial flow. Blood from the
RV will flow predominantly to the lungs, with only a small
percentage crossing to the aorta. These patients will be
neither significantly cyanotic nor symptomatic, because the
systemic and pulmonary blood flows will be nearly equal.
The narrowing of the RV outflow tract causes flow turbulence,
which results in the systolic ejection murmur that
usually brings these patients to attention.

With more severe obstructions in the pulmonary pathway,
pulmonary flow (Qp) will be significantly less than systemic
flow (Qs) as more systemic venous blood crosses to the aorta
through the VSD. The patient will present with cyanosis and
exertional dyspnea due to poor tissue oxygen delivery. With
exercise and increasing myocardial contractility, which can
narrow the subpulmonary area further, or with a rise in
pulmonary vascular resistance, the net resistance of the
pulmonary pathway may increase acutely, augmenting the
right-to-left shunt. This results in a precipitous drop in
pulmonary blood flow and profound episodic cyanosis, the
so-called “tet spell.” Patients with long-standing unrepaired
tetralogy of Fallot make behavioral adaptations to respond to
these physiological crises. With falling oxygen saturation,
they learn to squat, compressing the arteries in the lower
extremities, which raises the resistance of the aortic pathway
and restores the baseline level of pulmonary blood flow.

Indications for Intervention
Any patient with unrepaired tetralogy of Fallot should be
considered for intervention. By adulthood, they are typically
cyanotic, profoundly exercise intolerant, and polycythemic
and are at risk of arterial occlusion, hemoptysis, cerebral
abscess, and other life-threatening issues. When a complete
repair is anatomically and physiologically possible, correc-
tion of the defect provides the patient with a vastly superior
quality of life, although the surgery carries somewhat higher
mortality and morbidity in the adult than in the child. Palliative
procedures such as aorta-to–pulmonary artery
shunts and transcatheter balloon dilation of the RV outflow
tract may improve arterial saturation and reduce symptoms as
a result; however, experience with these palliations is princi-
ally in children. Acute increases in pulmonary blood flow
correspondingly increase pulmonary venous return, which
places an acute volume load on the LV. The less compliant
LV of the adult may not handle the volume load as easily as
the pediatric ventricle, and new symptoms of congestive heart
failure are possible.

Tetralogy of Fallot With Pulmonary Atresia
In the most severe cases of spiral septum malalignment, the
pulmonary valve may be atretic, or the main pulmonary artery
trunk may not form at all. In some of these newborns, the
ductus arteriosus may be the only source of pulmonary blood
flow (blood flows from the high-resistance aorta to the
lower-resistance pulmonary arteries). In the first few days of
life, as the ductus begins to close, these patients will become
profoundly cyanotic and will require medical intervention
(prostaglandin E1) to maintain ductal patency, followed by a
surgical reconstruction of the RV outflow tract.

Natural History
The resistance of the pulmonary path is extremely variable
from 1 patient to the next. If the obstructive lesions are mild,
the net resistance to pulmonary flow will be low compared
correct fusion with the growing muscular ventricular septum,
narrowing the pathway from RV to pulmonary artery and
enlarging the aortic root such that it extends over the RV
outflow tract. The RV hypertrophy is a secondary response to
increased afterload. Obstructions in the branch pulmonary
arteries, coronary anomalies, a right-sided aortic arch, and
additional VSDs are common additional associations.

In tetralogy of Fallot, systemic and pulmonary venous
return, the RA and LA, the atrial septum, and the AV valves
are typically normal. Blood ejected from the ventricles has 2
possible pathways: through the anatomically aligned outflow
tract or through the VSD to the opposite outflow. The
direction and magnitude of blood flow from each ventricle
will be determined by the relative resistance of each pathway.
With subpulmonary valvar obstruction, hypoplasia of the
pulmonary valve, narrowing of the main pulmonary artery
trunk, and the frequently associated branch pulmonary artery
stenoses, the pathway from the RV to the lungs in tetralogy of
Fallot is typically a high-resistance pathway (the net resis-
tance of obstructions in series is the sum of the individual
resistors). The combination of a high-resistance pulmonary
pathway and a nonrestrictive VSD creates the hemodynamic
conditions for significant right-to-left shunting at the ventric-
ular level, which results in systemic arterial desaturation.
In some patients with tetralogy of Fallot with pulmonary atresia, there may be no true (or visible) central pulmonary arteries. Major aortopulmonary (bronchial) arterial collaterals develop in utero to supply blood to the developing lungs. Frequently, a normal or nearly normal pulmonary blood flow is maintained. As a result, the diagnosis can be missed in the newborn period, because the infant has few symptoms. They are usually diagnosed later, when crying exacerbates their baseline hypoxemia or when continuous murmur in the lung fields are recognized. Because they are not ductal dependent, these patients may reach adulthood without intervention; however, in most cases, the collateral vessels fail to grow proportionally to the rest of the child. The vessels will become stenotic and create more resistance to pulmonary flow. Surgical or transcatheter augmentation of pulmonary blood flow may be required.

When collaterals are numerous and large enough, excessive pulmonary blood flow can lead to symptoms of congestive heart failure in infancy, potentially requiring medical, surgical, or transcatheter embolic therapy. With the natural tendency of the vessels to become stenotic, however, the symptoms often resolve as the child grows. In cases in which the individual collaterals are very large and short and do not become stenotic, the resistance of that pathway will remain very small. That segment of lung will be overperfused at high pressure relative to other segments. This can result in the unique physiology of segmental pulmonary vascular disease (Eisenmenger syndrome). Bull and associates in Great Britain have suggested that these patients may do equally well if left alone rather than undergoing a complex series of operations to reconstruct the pulmonary arteries and then close the VSD.

Patients With Prior Surgery in Childhood
Most adult patients with complex CHD will have undergone a prior (or multiple prior) intervention in early childhood and may present again as adults with new or persistent symptoms. This section will be limited to those patients with common lesions who have undergone restorative or definitive palliative procedures.

D-Transposition of the Great Arteries
D-transposition of the great arteries (D-TGA), another early embryological malformation, results in the embryological inversion of the great arteries in an otherwise normally developing heart. The aortic root is positioned anterior and to the right of the pulmonary artery (D transposed) and becomes the outlet for the RV. The pulmonary artery arises from the LV (Figure 4).

Unlike L-TGA, D-TGA most often occurs without associated cardiac anomalies and is incompatible with postnatal life. In patients with D-TGA, systemic and pulmonary venous return is normal, with normal atrial and ventricular connections; however, because the aorta arises from the RV, deoxygenated, systemic venous blood is returned directly to the aorta and to the body without passing through the lungs to become oxygenated. Similarly, because the pulmonary artery is the outlet for the left ventricle, pulmonary venous blood loops from the left heart to the lungs. Rather than 2 arterial circuits in series, the neonate with D-TGA has 2 separate independent circulations in parallel. Systemic oxygen saturation falls to very low levels within a few cardiac cycles, because it is not replenished. Anaerobic respiration ensues at the cellular level, which results in a profound systemic arterial acidosis. Without emergent intervention to improve oxygenation of the systemic arterial blood, the baby will die.

Because of the natural communications present at birth that allow the normal transition from the fetal to the postnatal circulation, the vast majority of infants with D-TGA will survive for hours or days. The ductus arteriosus allows for an aorta-to–pulmonary artery shunt with falling pulmonary vascular resistance. This additional pulmonary flow augments pulmonary venous return to the LA. With LA pressure higher than RA pressure, an LA-to–RA shunt can develop through the patent foramen ovale. This left-to-right flow brings oxygenated blood to the RA, which raises the oxygen content of the mixed blood that ultimately reaches the aorta. As long as the communication at the atrial level is adequate, and as long as LA pressure exceeds RA pressure, the baby can survive.

In some neonates, when the ductus arteriosus begins to close and pulmonary venous return falls, the favorable hemodynamics will change, and systemic oxygen levels will fall sharply. Reopening the ductus arteriosus with prostaglandin E1 will improve systemic oxygenation in this patient. In others, the flap valve of the PFO is more competent and severely limits left-to-right flow at the atrial level immediately after delivery. In these patients, even with a widely patent ductus arteriosus and a large shunt at that level, there will be little shunting at the atrial level, and systemic oxygenation will be inadequate. The first transcatheter inter-
in 1965 to 20 years after surgery, only 40% of patients with an atrial switch were in sinus rhythm. The presence of atrial tachyarrhythmias carries similar risks to that of other patients with sinus node dysfunction. Pacemaker and radiofrequency ablation therapy can be quite difficult due to the complexity of the atrial anatomy after this surgery. The “baffles” created within the pediatric atria may become obstructed with patient growth and may require surgical or interventional therapy to relieve symptoms of systemic or pulmonary venous obstruction. In intervening, care must be taken that enlargement of 1 pathway does not impinge on the pathway from the opposite set of veins. Small leaks in the baffles may also be present but are generally hemodynamically unimportant and are physiologically identical to small atrium-level shunts in other types of patients. Larger defects that allow significant shunting can be closed with transcatheter devices.

**“Natural History” After an Arterial Switch Operation**

In light of the restoration of normal anatomic connections, most children with the arterial switch operation have normal cardiac function and physiology. In a German series of 188
patients who underwent an arterial switch, survival was 91% at 10 years, with 96% of patients unlimited in their physical activity, and 99% taking no medication. Most clinical issues after the operation are the result of surgical residua from the initial operation in infancy.

Coronary lesions are rare, with myocardial ischemia very uncommon after reimplantation of the vessels. In a series of 755 arterial switch procedures, coronary perfusion issues were detected in 34 children, with documented ischemia in only 19. There are no data available yet on the risk of coronary complications later in adulthood.

The other major clinical issue after the arterial switch is related to anatomic distortion of the great vessels. Residual supravalvar stenosis at the aortic and pulmonary reanastomosis sites may be seen, but clinically significant obstructions are most often resolved in the pediatric age group with transcatheter or surgical therapy. Progressive dilatation and valvar insufficiency of the reconstructed aortic root may be problematic and may necessitate valve replacement later in life. Branch pulmonary artery stenosis may result from pulling the main pulmonary artery trunk forward to anastomose it to the former aortic root. This may be a clinically important afterload for the RV or may significantly redistribute pulmonary blood flow from 1 lung to the other if the degree of obstruction of the branches is unequal. These obstructive lesions have been treated successfully in the pediatric population with balloon and stent angioplasty. Because arterial switch patients are now reaching adulthood in growing numbers, the long-term outcome of Jatene’s operation continues to be unveiled.

“Natural History” After Surgical Intervention for Tetralogy of Fallot

In the late 1940s, before the era of open heart surgical repairs, palliative shunts were developed to carry blood directly from the aorta to the pulmonary artery, bypassing the obstruction in the RV outflow tract. The Blalock-Taussig shunt (subclavian to pulmonary artery), the Waterston shunt (direct anastomosis of ascending aorta to right pulmonary artery), and the Potts shunt (direct anastomosis of descending aorta to left pulmonary artery) were common in the 1950s and 1960s and enabled survival to adolescence and adulthood. Shunts were later used in the short-term palliation of neonates with severe cyanosis, so that complete open heart repairs could be performed more safely in an older/larger child.

Complete surgical repair of tetralogy of Fallot separates systemic and pulmonary venous return and creates unobstructed flow to both great arteries. Closure of the VSD is accomplished with an angled patch that directs LV flow to the aorta. Repair of the RV outflow tract and pulmonary arteries may entail subvalvar muscle resection, pulmonary valvotomy, transannular patching to enlarge a hypoplastic valve annulus, and patch angioplasty of the main or branch pulmonary arteries. Currently, corrective surgery is typically performed in the first year of life. With good surgical results, survival and quality of life have been excellent. In a retrospective analysis from the Mayo Clinic, 86% of patients were alive at 32 years, and in a series of 151 patients from Toronto, Canada, 94% were in New York Heart Association functional class I. Patients who have had only palliative shunts remain cyanotic and have many of the long-term issues of their counterparts who have not undergone repair (see above); however, in patients who have never undergone complete repair, longstanding or multiple shunt procedures may severely distort or interrupt the branch pulmonary arteries and may preclude more definitive repairs.

With a completed tetralogy of Fallot repair, normal cardiac physiology is restored. However, a number of hemodynamic issues may be seen in adults who have undergone surgical correction as children, including residual RV outflow obstruction, residual obstruction in the branch pulmonary arteries, residual shunts (at atrial, ventricular, or arterial levels), significant right-sided valvar insufficiency, aortic insufficiency, dilated and poorly contractile ventricles, heart block, and reentrant ventricular arrhythmia due to scarring in the ventricles. Sudden cardiac death may occur in patients with residual disease and may be predictable with electrophysiologic evaluation. Antitachycardia pacing may benefit some patients who are established to be at greatest risk for life-threatening arrhythmia.

Most often, adult tetralogy of Fallot patients present with new-onset or increasing exercise intolerance and must be evaluated to rule out both potentially important surgical residua and ventricular myocardial issues. RV dilatation and dysfunction are common in this group and are most often related to long-standing pulmonary regurgitation in patients who have had surgical manipulation of the valve. With dilatation of the RV and the tricuspid annulus, tricuspid regurgitation may be secondary but certainly compounds the issue of RV volume overload. The RV with preserved systolic function typically responds well to pulmonary valve replacement in many patients, with or without concurrent TV repair. LV dysfunction is common in patients who underwent surgery before 1970 and is most often related to suboptimal myocardial protection during surgery or to injury of unsuspected anomalous coronary branches. MRI has proven extremely valuable in the quantitative assessment of ventricular and valvar function in this population of patients who are typically difficult to image with transthoracic echocardiography due to surgical scarring and anatomic distortion. Patients who are free of clinical symptoms are frequently lost to follow-up, but ongoing care and screening are essential because the population remains at risk for ventricular dysfunction, ventricular arrhythmia, and, in some cases, sudden death.

The Adult Patient With Single-Ventricle Physiology (Fontan Operation)

Patients with functional single ventricles, those with absent or hypoplastic pumping chambers, absent or hypoplastic AV valves, or complex VSDs that cannot be closed, are reaching adulthood in large numbers for the first time. Simple palliations such as shunts or pulmonary artery banding were initially performed to maintain quality of life for a few years in patients with appropriate anatomy. Long-term survival was not seen until the introduction in 1971 of the Fontan operation, a more definitive palliative approach in which the systemic venous return is rerouted to completely bypass the
right heart. Initially used for patients with tricuspid atresia, the concept has now been applied to congenital lesions of all types in which the normal 2-ventricle circulation cannot be fully restored.

The current surgical approach to creating the Fontan physiology involves a staged rerouting of the systemic venous return. In the newborn period, a lesion-specific initial palliation will be performed, which, regardless of the initial anatomy, will leave the patient with a common physiology: complete mixing of systemic and pulmonary venous return, unobstructed pulmonary venous return to the ventricle, an unobstructed outflow tract to the systemic arterial circulation, and a limited but reliable source of pulmonary blood flow. These patients are able to survive to later palliation but face the physiological consequences of ongoing cyanosis (complete mixing of systemic and pulmonary venous blood) and a volume-loaded ventricle (which must have enough volume to pump blood to both the systemic and pulmonary circuits).

The second stage of palliation typically occurs between 3 and 6 months of life. A bidirectional Glenn shunt or hemi-Fontan procedure interrupts flow between the superior vena cava and the atrium and redirects superior vena cava flow directly to the pulmonary arteries. The creation of the cavopulmonary shunt improves the physiological conditions of the infant. Because blood from the inferior vena cava continues to mix with pulmonary venous return in the single ventricle, the patient remains desaturated. However, oxygenation of the deoxygenated systemic venous return is more efficient than when mixed arterial blood is delivered to the pulmonary artery, and the fraction of “blue” blood in the ventricle is smaller, which results in higher systemic oxygen saturations after the Glenn shunt (85% to 90%) than after the initial palliation. Finally, volume loading of the ventricle is eliminated because it pumps blood only to the systemic circulation.

The final stage of the palliation, the Fontan operation, redirects inferior vena caval flow away from the atrium to the pulmonary arteries, leaving only pulmonary venous blood to be pumped by the ventricle to the aorta (Figure 6). These patients become fully saturated after the surgery. Despite the complete separation of systemic and pulmonary venous blood, Fontan physiology is distinct from that of the normal heart.

In contrast to a 2-ventricle circulation, in which blood is pumped through 2 parallel circuits by separate pumps, the single functional ventricle in a Fontan circulation must generate enough energy to push blood through both the systemic and pulmonary vascular beds consecutively. There is no energy added by a second ventricle to help push blood through the lungs. Flow from the systemic veins, through the lungs and back to the ventricle, is entirely passive (Figure 7). Low resistance in this pathway is therefore critical. Anatomic obstructions in the pulmonary vasculature, elevation of pulmonary vascular resistance, competitive arterial flow into the lungs, AV valve stenosis or regurgitation, elevation of ventricular end-diastolic pressure, or rhythm disturbances with loss of AV synchrony may create critical impedance to flow.

Figure 6. External conduit-type Fontan operation in a patient with pulmonary atresia and hypoplastic RV. Superior vena cava (SVC) is disconnected from RA and connected directly to pulmonary artery (bidirectional Glenn shunt), and inferior vena cava (IVC) flow is rerouted through external conduit directly to pulmonary artery. Systemic venous blood (black arrows) flows to lungs; only pulmonary venous blood is pumped to aorta (Ao; white arrow). RPA indicates right pulmonary artery; LPA, left pulmonary artery.

“Natural History” of a Fontan Circulation

Today, children with Fontan physiology are reaching adulthood in unprecedented numbers. Initially after the surgery, >90% of patients are in New York Heart Association class I or II, with marked improvements in exercise capacity (compared with their preoperative state) due to improved tissue oxygen delivery. Unlike patients with repairs of simple defects such as patent ductus arteriosus or ASD, Fontan patients experience ongoing attrition even after decades of symptom-free survival. This is due to ventricular failure; breakdown and growth-related senescence of constructed pathways; the development of atrial arrhythmia; fluid retention and electrolyte disturbances; low cardiac output; and thrombotic and thromboembolic issues. The classic paper by Fontan et al in the early 1990s proved the palliative, rather than reparative, nature of the procedure. In that series, after 12 years, only 70% of “perfect” Fontan patients were alive, and fewer than half of the survivors remained in New York Heart Association class I or II.

Advances in the pre-Fontan management of these children, including staging of surgical reconstruction and improved surgical techniques, are likely to have resulted in better late outcomes since the Fontan paper was published, but it is clear that the procedure will never be curative in nature. Although...
the acute surgical management of these patients remains a pediatric cardiology issue, the long-term effects of this unusual cardiac physiology are increasingly confronting adult cardiologists.

**Indications for Intervention**

As described above, any circulatory issue that increases the pathway resistance from the systemic veins back to the ventricle will impede the passive flow of the Fontan, leading to higher systemic venous pressures. Most often, this results in a spectrum of symptoms typical of a patient with classic “right heart failure”: systemic venous congestion, fluid retention (particularly peripheral edema, ascites, and pleural and pericardial effusions), and low cardiac output due to reduced systemic ventricular preload.

Alternatively, patients with increased pathway resistance may decompress the Fontan circuit through the development of venous collaterals from the higher-pressure Fontan pathway to the lower-pressure pulmonary veins or LA. This right-to-left shunt will lower the Fontan pathway pressure and maintain ventricular preload but will result in increasing cyanosis. Rising pathway pressures may also create increasing right-to-left flow through existing residual defects in the surgically constructed pathway inside the atria.

When clinical symptoms bring Fontan patients to attention in an adult cardiology setting, skilled assessment is required in the catheterization laboratory. In congested low-output patients, small pressure gradients across venous connections, not readily detectable by noninvasive techniques, may represent a significant resistance to flow. Such obstructions in the branch pulmonary arteries and at suture lines may be balloon dilated or stented to minimize resistance to forward flow.\(^{57,58}\)

Coil embolization of aorta to pulmonary artery collaterals should be performed to eliminate high-pressure competitive flow, when identified. AV synchrony should be restored with the use of medications or a pacemaker for patients who are bradyarrhythmic or in junctional rhythm. In cyanotic patients, careful angiographic evaluation of the Fontan pathway is critical. Embolization of venous collaterals or device closure of intracardiac defects may be beneficial,\(^{59}\) but elimination of the right-to-left shunt may exacerbate symptoms of low output and venous congestion by eliminating the “pop-off” valve from the high-resistance pulmonary circuit.

When no treatable anatomic issues are identified, medical management is extremely limited for the patient with a failing Fontan circulation. In some cases, normal changes in ventricular compliance that occur with aging may increase end-diastolic pressures sufficiently to cause venous pathway congestion. The creation of a Fontan fenestration (a shunt at the atrial level) may be performed surgically or in the catheterization laboratory\(^{59,60}\) as a further palliation, often as a bridge to transplantation. Although some degree of cyanosis is created, this intervention will increase both cardiac output and tissue oxygen delivery. Physiologically, this mimics the creation of a small ASD in patients with end-stage pulmonary hypertension.\(^{61}\)

Cardiac transplantation is a last option for the failing Fontan. In general, transplantation is extremely well tolerated physiologically in this population. Pulmonary hypertension is never an issue as it is in cardiomyopathy patients, because Fontan patients have survived with only passive pulmonary flow. However, the complexity of reconstructing the systemic and venous connections and the pulmonary arterial pathways, along with the scarring from multiple prior cardiac surgeries, makes the transplant operation itself extraordinarily challenging.

**Conclusions**

CHD in the adult population, more than any other type of malformation, is taxing the current medical system, because the number and complexity of patient issues are outgrowing the limited facilities established to care for them. With better survival from childhood, it is evident that few of our surgical and catheter-based interventions are curative and that a lifetime of care will be required. The education of both internal medicine/cardiology trainees and those already in practice, as well as the development of national databases for tracking patients and their responses to therapy are critical to the future care of this complex and diverse population. Clinical systems designed for the transition of these patients out of the pediatric clinics where many continue to receive their care and into organized, regional centers of excellence for adult patients with CHD will facilitate this process.

**Disclosures**

None.
References


25. Chandler JS, Silversides C, Harris L, Webb GD, Siu SC, Therrien J. Left ventricular dysfunction is a risk factor for sudden cardiac death in adults...
late after repair of tetralogy of Fallot. J Am Coll Cardiol. 2002;40:
1675–1680.
45. Geva T, Sandweiss BM, Gauvreau K, Lock JE, Powell AJ. Factors
associated with impaired clinical status in long-term survivors of
tetralogy of Fallot repair evaluated by magnetic resonance imaging. J Am
46. Gatzoulis MA, Balaji S, Webber SA, Siu SC, Hokanson JS, Poile C,
Rosenthal M, Nakazawa M, Moller JH, Gillette PC, Webb GD, Reddington
AN. Risk factors for arrhythmia and sudden cardiac death late after repair
47. Khairy P, Landzberg MJ, Gatzoulis MA, Lucron H, Lambert J, Marçon F,
Alexander ME, Walsh EP. Value of programmed ventricular stimulation
48. Gatzoulis K, Frogoudaki A, Brili S, Stefanadis C. Implantable defibril-
lators: from the adult cardiac to the grown up congenital heart disease
Pulmonary valve replacement in adults late after repair of tetralogy
Fallot: are we operating too late? J Am Coll Cardiol. 2000;36:1670–1675.
50. Geva T, Sandweiss BM, Gauvreau K, Lock JE, Powell AJ. Factors
associated with impaired clinical status in long-term survivors of
tetralogy of Fallot repair evaluated by magnetic resonance imaging. J Am
52. Jacobs ML, Rychik J, Rome JJ, Apostolopoulou S, Pizarro C, Murphy JD,
Norwood WI Jr. Early reduction of the volume work of the single
456–461.
53. Woods RK, Dyamenahalli U, Duncan BW, Rosenthal GL, Lupinetti FM.
Comparison of extracardiac Fontan techniques: pedicled pericardial
125:465–471.
SD, Newburger JW, Wernovsky G. Functional outcome after the Fontan
1997;114:392–403.
55. Fontan F, Kirklin JW, Fernandez G, Costa F, Naftel DC, Tritto F,
Blackstone EH. Outcome after a “perfect” Fontan operation. Circulation.
56. de Leval MR. The Fontan circulation: What have we learned? What to
57. McMahon CJ, El Said HG, Vincent JA, Griñka RG, Nihill MR, Ing FF,
Fraley JK, Mullins CE. Refinements in the implantation of pulmonary
arterial stents: impact on morbidity and mortality of the procedure over
the last two decades. Cardiol Young. 2002;12:445–452.
58. Sugiyama H, Yoo SJ, Williams W, Benson LN. Characterization and
treatment of systemic venous to pulmonary venous collaterals seen after
59. Kreutzer J, Lock JE, Jonas RA, Keane JF. Transcatheter fenestration
dilation and/or creation in postoperative Fontan patients. Am J Cardiol.
60. Rychik J, Rome JJ, Jacobs ML. Late surgical fenestration for compli-
balloon atrial septostomy in patients with severe primary pulmonary

Key Words: transposition of great vessels ■ tetralogy of Fallot ■ Fontan
procedure ■ heart defects, congenital
Pathophysiology of Congenital Heart Disease in the Adult: Part III: Complex Congenital Heart Disease

Robert J. Sommer, Ziyad M. Hijazi and John F. Rhodes

Circulation. 2008;117:1340-1350
doi: 10.1161/CIRCULATIONAHA.107.714428

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2008 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/117/10/1340

An erratum has been published regarding this article. Please see the attached page for:
/content/119/21/e547.full.pdf

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/
In the article by Sommer et al, “Pathophysiology of Congenital Heart Disease in the Adult: Part III: Complex Congenital Heart Disease,” which appeared in the March 11, 2008, issue of the journal (Circulation. 2008;117:1340–1350), the following correction should be made:

On page 1342, toward the top of the right column, the statement, “Resting ECGs typically have a q wave in the left precordial leads (due to anatomic reversal of the septum itself) . . .” is incorrect, and the sentence should be replaced by, “The septum (and the conduction system tissue that runs through it) is reversed, such that depolarization of the septum occurs from right to left (morphologic LV to morphologic RV). This typically produces a qS pattern in the right-sided precordial leads and the absence of Q waves in the left precordial leads.”

This change has been made to the current online version of the article. The authors regret the error would like to thank several astute readers for pointing out the mistake.

DOI: 10.1161/CIRCULATIONAHA.109.192577