Cardiology in the Young (2012), **22**, 768–779
doi:10.1017/S104795111200203X

Original Article

Long-term management of adults with conotruncal lesions: the diagnostic approach at All Children's Hospital*

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Abstract Improved survival in children with complex congenital cardiac disease, such as conotruncal abnormalities, has created a sub-population of children and young adults who need comprehensive multi-disciplinary long-term follow-up. Routine surveillance with comprehensive screening for structural heart disease, functional heart disease, thromboembolic disease, arrhythmias, and associated end-organ dysfunction is important. Future research will better define the care plans for routine surveillance in patients with conotruncal abnormalities.

Keywords: Adult congenital heart disease; conotruncal; common arterial trunk; transposition of the great arteries; tetralogy of Fallot; DiGeorge syndrome

Conotruncal abnormalities are a major form of complex congenital cardiac disease that requires comprehensive multi-disciplinary management throughout the lifetime of an individual. Conotruncal abnormalities may be defined as any anomaly that affects the embryological development of the common arterial trunk and muscular conal tissue. These structures initially reside over the right ventricle in the developing heart. During embryological development, these structures proceed to septate and rotate to create a leftward aorta, a rightward pulmonary artery, and an intact ventricular septum. Approximately 20–30% of all forms of congenital cardiac disease will involve the cardiac outflow tracts, aortic arch, arterial duct, and proximal pulmonary arteries. Common forms of conotruncal congenital cardiac disease typically include:

- common arterial trunk,
- tetralogy of Fallot,
- transposition of the great arteries,
- double-outlet right ventricle,
- pulmonary atresia and ventricular septal defect,
- interrupted aortic arch with ventricular septal defect, and
- hemi-truncus.

The aetiology of conotruncal anomalies results from abnormalities of neural crest cell migration or disruption of the secondary heart field during heart tube development early in embryogenesis. Most infants born with conotruncal abnormalities will not survive without surgical intervention. Advances in paediatric and neonatal cardiac surgery and interventional cardiology have improved survival, and today more that 90% of infants born with congenital cardiac disease will survive to adulthood. The goal of surgical intervention for conotruncal

*Presented at the 12th Annual International Symposium on Congenital Heart Disease, February 17–21, 2012 at All Children's Hospital, Saint Petersburg, Florida, United States of America.

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abnormalities is to re-establish biventricular physiology through:

- closure of the ventricular septal defect, if present;
- creation of unobstructed blood flow across the right ventricular outflow tract; and
- creation of an unobstructed blood flow across the left ventricular outflow tract.

The type of surgical approach varies based on the specific lesion. In 2011, the Society of Thoracic Surgeons Congenital Heart Surgery Database reported overall mortality before discharge from the hospital after surgical repair for patients with common forms of conotruncal disease in the United States and Canada:[1]

- Repair of tetralogy of Fallot (1.1%),
- arterial switch procedure for transposition of the great arteries (2.9%),
- arterial switch procedure and ventricular septal defect closure for transposition of the great arteries and ventricular septal defect (7.0%), and
- repair of common arterial trunk (10.9%).

Following surgical repair or palliation, patients may have a variety of residual or recurrent lesions:

- residual or recurrent intracardiac shunts,
- right ventricular outflow tract obstruction,
- pulmonary valvar stenosis or regurgitation;
- left ventricular outflow tract obstruction,
- aortic valvar stenosis or regurgitation, or
- aortic root dilation.

The longitudinal follow-up of patients with conotruncal lesions as they enter adolescence or adulthood requires a basic structural assessment for:

- any residual atrial or ventricular level shunts;
- complete assessment of the right ventricular outflow tract;
- complete assessment of the left ventricular outflow tract; and
- surveillance for arrhythmias.

Physicians who provide the long-term management of patients with conotruncal abnormalities require a thorough understanding of the inherent morbidities associated with the native cardiac disease and the acquired morbidities that can develop over a lifetime. Surgical approaches to conotruncal abnormalities are not a cure; they are just palliative procedures for an otherwise lethal disease. Clinicians caring for patients with conotruncal abnormalities therefore need to be astute to the development of a variety of potential complications:

- complications from underlying genetic abnormalities,
- structural cardiac disease,
- functional cardiac disease,
- electrical conduction disorders,
- thromboembolic disease,
- associated end-organ dysfunction, and
- complications associated with pregnancy.

The early recognition of these findings may allow for early medical or surgical intervention that may improve the overall quality of life. The continued development of centres of excellence with comprehensive teams of medical and surgical providers dedicated to caring for children and adults with congenital heart disease is needed. In the future, the development of plans of care that allow for routine surveillance for these issues is needed to standardise care throughout the country. Below we describe the diagnostic approach of the multidisciplinary team at our centre for the long-term care of patients with conotruncal abnormalities. Separate articles within this HeartWeek Supplement will address multiple related topics, including:

- the anatomical diagnosis,
- surgical and catheterisation-based interventions, and
- the management of arrhythmias.

Genetics

Advances in molecular biology and genetics continue to enhance our understanding of the molecular determinants of cardiac development. Many forms of congenital cardiac disease are not due to single gene defects but are most likely multi-gene abnormalities in transcriptional pathways of human development that may lead to a common phenotype. The incidence of common conotruncal abnormalities was estimated by Long et al in infants without obvious syndromic features:[2–7]

- common arterial trunk: 0.35 per 10,000 live births,
- transposition of the great arteries: 1.98 per 10,000 live births, and
- tetralogy of Fallot: 2.4 per 10,000 live births.

In comparison, DiGeorge syndrome, the most common microdeletion syndrome, affects ~1 in 4000–6000 live births and may predispose to conotruncal abnormalities.[2–7] DiGeorge syndrome is an excellent example of transcriptional dysregulation. DiGeorge syndrome is characterised by deletion on chromosome 22q11. This deletion leads to loss of a transcriptional protein (TBX1) that is important for development of secondary heart field, myocardium of the cardiac outflow tract, and differentiation of the neural crest cells.[2–7] DiGeorge syndrome is characterised by the triad of conotruncal congenital

https://doi.org/10.1017/S104795111200203X Published online by Cambridge University Press

Table 1. DiGeorge syndrome summary.

Diagnosis	Abnormal development of the pharyngeal pouches creating a classic triad of clinical findings: conotruncal congenital heart disease, hypoplasia of the thymus, and hypocalcaemia
	Partial DiGeorge syndrome: non-life-threatening immunological defects
	Complete DiGeorge syndrome: severe life-threatening immunological defects
Genetics	90% will have a heterozygous deletion of chromosome 22q11.2
	<5% have heterozygous deletion of chromosome 10p13-14
Cardiac	Common arterial trunk
	Tetralogy of Fallot
	Interrupted aortic arch
	Atrial or ventricular septal defects
	Vascular rings
Head–Eyes–Ears–Nose–Throat	Thymic hypoplasia
	• Immunodeficiencies due to T- and B-cell function
	Palatal abnormalities
	• High arched palate, cleft palate, submucosal cleft, velopharyngeal incompetence, bifid uvula
	Nasal dysmorphism
	Other: wide nasal bridge, short philtrum, low-set and posteriorly rotated ears, and ocular hypertelorism
Endocrine	Hypoplasia of the parathyroid glands
	• Hypocalcaemia
	• Hypophosphatemia
	• Common in infancy but many times stabilises in adults as the remaining parathyroid tissue develops compensatory hyperplasia
	Autoimmune thyroid dysfunction
	Growth hormone deficiency
Allergy–Immunology	Autoimmune-related cytopenias
	Allergic rhinitis/atopy
	Autoimmune-related arthritis
	Malignancy related to immunodeficiency
Neurodevelopmental	Learning disabilities
	Speech delay
	Schizoaffective disorder/schizophrenia
	Depression
Renal	Renal abnormalities
	Increased need for post-operative dialysis

cardiac disease, hypoplasia of the thymus, and hypocalcaemia. DiGeorge syndrome actually exists within a wide spectrum of phenotypic expression. Table 1 provides a summary table of the abnormalities that may exist in DiGeorge syndrome. Many adults may not have undergone genetic testing in childhood because it was not available at that time and may have unrecognised DiGeorge syndrome. Practitioners need to be able to recognise the clinical features of DiGeorge syndrome and screen high-risk populations of adult congenital patients, including those with

- common arterial trunk,
- tetralogy of Fallot,
- interrupted aortic arch,
- atrial or ventricular septal defects, and/or
- vascular rings.

Identification of these unrecognised adults is important in order to provide healthcare services that include:

- reproductive counselling, and
- surveillance for extracardiac malformations, including thyroid/parathyroid disorders, immunodeficiencies, renal abnormalities, and neurobehavioural/psychiatric issues.

In order to accommodate for these issues, we have developed a collaborative cardiovascular genetics clinic for patients who require genetic evaluation and counselling within our heart institute.

Structural and functional heart disease

The anatomical surveillance of a patient with a conotruncal abnormality starts with a thorough understanding of the prior surgical and catheterisation procedures performed. Before any clinic visit, all old reports are requested. Important factors to be aware of in the management of these complex patients include:

- the location where the prior procedure was performed – that is, the institution,
- the approach used – catheterisation site, thoracotomy versus median sternotomy, and

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- operative or catheterisation note describing the procedure in detail.

Medical providers always need to consider the flow of blood through a segmental approach in order to determine the possible structural abnormalities. Table 2 is a list of the potential residual structural anomalies that may exist in congenital cardiac patients with conotruncal abnormalities. Structural abnormalities may also be acquired in adults with conotruncal lesions due to:

- vascular thrombosis,
- endocarditis,
- development of pulmonary hypertension,
- chemotherapy, or
- pregnancy.

Table 2. Segmental approach to assess for residual structural cardiac anomalies in the long-term surveillance of adults with conotruncal abnormalities.

Cardiac segment	Anomaly
Systemic veins	• Vascular thrombosis from previously placed lines
	• Left superior caval vein
Right atrium	• Right atrial dilation due to progressive tricuspid regurgitation or intracardiac shunt (atrial septal defect or partial anomalous pulmonary vein)
Tricuspid valve	• Tricuspid regurgitation
	• Associated dysplasia of the valve
Right ventricle	• Right ventricular dilation due to progressive pulmonary regurgitation and/or associated tricuspid regurgitation
	• Residual right ventricular outflow tract obstruction
	• Right ventricular outflow tract aneurysm due to previously placed surgical patches
	• Systolic dysfunction
	• Diastolic dysfunction
	• Asynchrony from electrical conduction disturbance
Pulmonary valve	• Regurgitation
	• Stenosis
Pulmonary hypertension	• Assessment for pulmonary hypertension (tricuspid regurgitation jet, septal configuration, pulmonary regurgitation jet, right ventricular hypertrophy, right ventricular function)
Branched pulmonary arteries	• Right or left peripheral pulmonary stenosis
Pulmonary veins	• Partial anomalous pulmonary venous return
Atrial septum	• Residual atrial level shunt (atrial septal defect/patent foramen ovale)
Mitral valve	• Regurgitation
	• Stenosis
Left ventricle	• Left ventricular dilation due to progressive aortic regurgitation and/or associated mitral regurgitation
	• Development of left ventricular outflow tract obstruction
	• Systolic dysfunction
	• Diastolic dysfunction
	• Asynchrony from electrical conduction disturbance
Aortic valve	• Dysplasia
	• Regurgitation
	• Stenosis
Aortic root	• Neo-aortic root dilation
	• Aneurysm formation
Aorta	• Arch sidedness
	• Arch vessel anomalies (aberrant right or left subclavian arteries)
	• Coarctation
Collaterals	• Veno-venous collaterals
	• Arteriovenous collaterals
Other	• Intracardiac thrombus
	• Endocarditis

https://doi.org/10.1017/S104795111200203X Published online by Cambridge University Press

Multiple imaging modalities may be needed to provide a complete anatomical surveillance in patients with conotruncal congenital cardiac disease, including:

- transthoracic echocardiography,
- trans-oesophageal echocardiography,
- three-dimensional echocardiography,
- cardiac computed tomography angiography,
- cardiac magnetic resonance imaging, and
- cardiac catheterisation with angiography.

We utilise transthoracic echocardiography with a complete congenital segmental assessment in all patients with conotruncal lesions every 6 to 12 months.

Table 2 reviews the segmental approach to surveillance of structural defects in children or adults with conotruncal congenital heart disease and Table 3 reviews the advantages and disadvantages of these particular diagnostic tests. The systemic veins and atrial septum can be difficult to delineate in

Table 3. Diagnostic testing used in the long-term surveillance in patients with conotruncal forms of congenital heart disease.

Mode of surveillance	Advantages	Frequency
Office visit/physical exam		Every 6–12 months
Electrocardiogram	Screen for conduction abnormalities	Every 6–12 months
Holter monitor	Screen for conduction abnormalities	Annually
Exercise stress test	Screen for conduction abnormalities or ischaemic changes related to coronary artery abnormalities	As clinically indicated – see below: All patients during puberty with transposition of the great arteries to assess for ischaemia related to coronary ostial stenosis All patients with pulmonary regurgitation (common arterial trunk/ tetralogy of Fallot) may benefit from assessment of the peak oxygen consumption to assess their functional capacity prior to consideration of pulmonary valve replacement
Echocardiogram	Screen for structural anomalies, pulmonary hypertension and changes in heart function	Every 6–12 months
Three-dimensional echocardiography	Helpful in the assessment of valve regurgitation; especially in the evaluation of an aortic or truncal valve	As clinically indicated
Trans-oesophageal echocardiography	Assessment of systemic veins, pulmonary veins, atrial septum, valvar abnormalities, and thrombus formation	As clinically indicated
Cardiac magnetic resonance imaging/angiography	Good assessment of thoracic vascular structures such as: branched pulmonary arteries, pulmonary veins, and aortic arch. Gold standard for functional assessment and quantification the size of the right ventricle. May not be able to be performed in patients with pacemakers or who have previously had implanted stents/coils	As clinically indicated
Cardiac computerised tomographic scan/ angiography	Good assessment of thoracic vascular structures such as: branched pulmonary arteries, pulmonary veins and aortic arch. Good assessment of pulmonary parenchyma. Maybe performed with previously placed pacemakers or stents/coils	As clinically indicated
Laboratory values	Lipid panel	Annual
Additional laboratory values to consider	Liver function tests (Aspartate Aminotransferase [AST] and Alanine Aminotransferase [ALT]) Basic chemistry (calcium) Brain natruretic peptide D-Dimer Thyroid function tests	As clinically indicated
Pulmonary function tests	Specially consider in patients with significant scoliosis or chest wall deformities, or if on amiodarone for arrhythmias	As clinically indicated
DiGeorge syndrome	Thyroid function tests Parathyroid function (serum calcium and phosphorus) Monitoring of T- and B-cell function • Flow cytometry for immune cell enumeration • In vitro proliferation assay to assess for T-cell function • Total immunoglobulin levels • Specific antibody titres	Every 6–12 months

https://doi.org/10.1017/S104795111200203X Published online by Cambridge University Press

older children and adults by transthoracic imaging. In these cases, trans-oesophageal echocardiography and magnetic resonance imaging may be useful. The knowledge of vascular patency is important before scheduling a cardiac catheterisation or planning an interventional procedure. A residual atrial level shunt is important as this can lead to progressive right ventricular dilation and also be a source for a paradoxical embolic stroke. A residual atrial level shunt is also a contraindication to placement of a transvenous pacing wire or automatic implantable cardiac defibrillator due to the risk of embolic stroke. Many patients who have had neonatal surgical repair or palliation may have a patent foramen ovale left intentionally open because of concerns for elevated right ventricular pressure or pulmonary hypertension in the post-operative period.

Patients with a common arterial trunk and tetralogy of Fallot are particularly at risk of developing progressive right ventricular dilation due to pulmonary regurgitation. Standard approaches to surgical intervention in these patient groups include closure of the ventricular septal defect and creation of a right ventricular outflow tract, which in many cases develops pulmonary regurgitation or stenosis over time. The accurate assessment of the right ventricular size and function is necessary to determine the timing of replacement of the pulmonary valve in these individuals. The best measure of right ventricular size is by cardiac magnetic resonance imaging,[8,9] which is done non-invasively without radiation exposure. The three-dimensional images allow assessment and quantification of:

- right ventricular volume,
- right ventricular systolic function,
- regurgitation fraction, and
- structural assessment of the tricuspid valve, right ventricular outflow tract, pulmonary valve, branches of the pulmonary arteries, and pulmonary veins.

The cost of cardiac magnetic resonance imaging/angiography is a limiting factor, and advances in three-dimensional echocardiography have demonstrated good specificity when correlating three-dimensional volume assessments between magnetic resonance imaging and echocardiography for the right ventricle.[8,9] Right ventricular volumes $> 150–170\ ml/m^2$ are typically used as cut-offs to consider surgical or catheter-based replacement of the pulmonary valve. These imaging modalities are also good at detecting right ventricular outflow tract aneurysms that may develop around previously placed right ventricular outflow tract patches or along the suture lines of replaced pulmonary valves.

Stenosis of the branches of the pulmonary arteries is also common in all forms of conotruncal congenital cardiac disease, including common arterial trunk, tetralogy of Fallot, and transposition of the great arteries. In patients with a common arterial trunk, the main pulmonary artery or branch pulmonary arteries are removed from the ascending aorta and connected to a pulmonary conduit – polytetrafluoroethylene, homograft, or porcine) or the right ventricle, thereby creating the risk of supravalvar pulmonary stenosis or proximal branched pulmonary artery stenosis. In tetralogy of Fallot, residual pulmonary stenosis may exist at any point along the right ventricular outflow tract, including infundibular, valvar, supravalvar, or peripheral pulmonary stenosis. Patients with transposition of the great arteries in comparison typically have discrete proximal peripheral pulmonary stenosis due to tension placed on the proximal pulmonary arteries during the Lecompte manoeuvre. The pulmonary valve and main pulmonary artery are typically seen by transthoracic echo imaging. The branches of the pulmonary arteries are usually not well seen by transthoracic imaging in adolescents and adults. Alternative non-invasive imaging modalities to better delineate the peripheral pulmonary arteries and pulmonary vasculature include cardiac magnetic resonance angiography and computed tomographic angiography. Computed tomographic angiography is commonly used in patients who have had previously placed stents, coils, pacemakers, or automatic implantable cardiac defibrillators, owing to the artefacts associated with magnetic resonance imaging. Lung perfusion scans may also be helpful in the quantification of the flow of blood in the pulmonary circulation.

Assessment of the left ventricle and left ventricular outflow tract is also important. All repaired adult patients with tetralogy of Fallot or common arterial trunk, and some patients with transposition of the great arteries, will have previously undergone closure of a ventricular septal defect. The recognition of a residual ventricular level shunt is typically detected by auscultation and usually well imaged by transthoracic echocardiography. Residual ventricular septal defects may cause left atrial and left ventricular dilation and be a nidus for endocarditis. The development of left ventricular dysfunction is a significant risk factor for early and late morbidity and mortality in patients with conotruncal congenital heart disease. The left ventricular function in conotruncal abnormalities can be affected by a number of factors:

- idiopathic developmental issues with the myocardium;

https://doi.org/10.1017/S104795111200203X Published online by Cambridge University Press

- increased work load due to progressive left ventricular outflow tract obstruction, systemic hypertension, volume loading from residual ventricular shunts, mitral regurgitation, or aortic regurgitation;
- myocardial ischaemic injury from coronary artery abnormalities;
- hypoxic injury to multiple episodes of cardiopulmonary bypass; or
- septal shift due to right ventricular dilation.

Left ventricular systolic and diastolic functions are commonly assessed in the outpatient setting with transthoracic echocardiography. The utilisation of new echocardiography modalities, such as tissue Doppler and speckle tracking in two-dimensional or three-dimensional imaging, allows for further assessment of left ventricular functional parameters such as strain, strain rate, and torsion.[10] In 2012, Diller et al demonstrated that two-dimensional left ventricular global strain was an independent risk factor for sudden cardiac death in adults with tetralogy of Fallot.[11,12] Acquired left ventricular dysfunction may occur because of congenital coronary arterial anomalies, such as a single coronary artery or anomalous origin of the coronary artery. In addition, patients with transposition of the great arteries who have undergone an arterial switch procedure may develop stenosis of the ostium of the coronary arteries owing to the previous translocation of the coronary arteries at the time of surgery. The utilisation of exercise stress tests or nuclear stress tests may help delineate this aetiology in patients with clinical symptoms. Anatomical diagnosis may be made by computed tomographic angiography, but cardiac catheterisation with angiography of the coronary arteries is commonly required in order to make a definitive diagnosis.

The aortic valve or common arterial valve can have associated dysplasia in patients with conotruncal abnormalities. The degree of stenosis or regurgitation needs to be closely followed by practitioners longitudinally over a patient's lifetime. Patients with conotruncal lesions are also at risk of developing progressive dilation of the aortic root, which may be secondary to:

- malalignment of the ventricular septum,
- turbulence across the aortic or truncal valve, or
- the inherent make-up of the vascular smooth muscle and endothelium.

The size of the aortic root and aortic arch can be followed by serial echocardiography, computerised axial tomography, or magnetic resonance imaging. Aortic root dilation rarely progresses to dissection and/or rupture, unlike the dilation of the aortic root in connective tissue disorders such as Marfan syndrome. In 2010, Stulak et al reported that adult patients with conotruncal abnormalities commonly had moderate ascending aortic enlargement, with a median diameter of 45 mm, but dissection was rare.[12,13] The indications for replacement of the aortic root are typically related to the development of aortic regurgitation and progressive left ventricular dilation.

The surveillance of structural cardiac disease in adults with conotruncal congenital cardiac disease requires an experienced team of individuals trained in congenital cardiac disease, including:

- physicians,
- nurses,
- echocardiographic sonographers, and
- advanced cardiac imaging technicians.

Transthoracic echocardiography is a useful non-invasive method of routine surveillance for patients with conotruncal congenital cardiac disease. Transoesophageal and three-dimensional echocardiography may also be helpful adjuncts. Cardiac magnetic resonance imaging and computed axial tomography are best reserved for periodic assessment approximately every 3 to 5 years, or sooner if clinically indicated in adults with conotruncal congenital cardiac disease.

Surveillance for arrhythmias

All adults with congenital cardiac disease are at potential risk of developing late atrial or ventricular arrhythmias. Please see the separate article in this HeartWeek Supplement that addresses this topic in more detail. We utilise an electrocardiogram at routine clinic visits and an annual Holter monitor for surveillance of possible arrhythmias. Exercise stress tests may also be useful in these patients to

- assess for subclinical arrhythmias,
- assess for ischaemic changes related to abnormalities of the coronary arteries, and
- assess the functional capacity by measurement of peak oxygen consumption.

Please see Table 3 for a summary of these recommendations.

Additional surveillance of end organs

Evaluation of the function of end organs may be just as important as the cardiac structural and functional assessment in patients with conotruncal congenital cardiac disease. The surveillance of end-organ dysfunction in patients with conotruncal congenital cardiac disease requires physicians to use a systematic approach (Table 4). Medical providers can think of this as a head-to-toe assessment of the body.

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Table 4. Non-cardiac end organ dysfunction due to conotruncal abnormalities.

Body Part	Complications
Central nervous system	Seizure, stroke, motor delays, learning disabilities
Head–Eyes–Ears–Neck–Throat	Vocal cord dysfunction
	Chronic otitis media/hearing loss
	Sinusitis
	Oral feeding intolerance
	Speech delay
Respiratory	Chronic lung disease/reactive airway disease
	Restrictive lung disease due to scoliosis
	Pulmonary fibrosis from medications (amiodarone)
	Tracheobronchomalacia
Gastrointestinal	Gastro-oesophageal reflux
	Oesophageal varices if portal hypertension
	develops from liver cirrhosis
	Failure to thrive
Endocrine	Thyroid dysfunction
	Parathyroid dysfunction
	Failure to thrive/growth restriction
Musculoskeletal	Scoliosis
Haematology	Hypercoaguable state
	Thromboemboli
Allergy–Immunology	T-cell dysfunction
	B-cell dysfunction
	Atopic dermatitis
	Allergic rhinitis/sinusitis
Renal	Congenital renal abnormalities

Constitutionally, practitioners need to consider the presence of a possible genetic disorder such as DiGeorge syndrome or another syndrome. Consideration of a genetic aetiology may be triggered by the presence of:

- multiple congenital anomalies,
- failure to thrive,
- short stature, or
- developmental delays.

In DiGeorge syndrome, ~90% will have a deletion of chromosome 22q11, but additional genetic defects produce similar phenotypes such as 10p13-14 deletion. At All Children's Hospital, we typically perform screening chromosomal microarray in the neonatal period to exclude DiGeorge syndrome or other associated genetic abnormalities. Any adult patient with conotruncal congenital cardiac disease and clinical features of DiGeorge syndrome without genetic confirmation should have a chromosomal microarray sent.

The central nervous system can be affected in patients with conotruncal abnormalities owing to the congenital disease, foetal cyanosis, seizure, stroke, and global ischaemic injury. These patients are at risk for seizures and developmental delays including motor delays and learning delays. All patients who have had cardiac surgical repair or palliation are at risk for arrhythmias and conduction disorders; therefore, any new onset seizures or syncope should warrant a complete neurological and electrophysiological evaluation. As they age, patients with DiGeorge syndrome may also develop schizoaffective disorder, schizophrenia, and depression. Patients with conotruncal congenital cardiac disease commonly have neurodevelopmental issues. Speech delays are common owing to the palate or vocal cord issues discussed below. Developmental delays and learning disabilities may be secondary to cyanosis in foetal life or part of larger developmental abnormalities.

The head–eyes–ears–nose–neck–throat can be affected in many ways. Patients with DiGeorge syndrome may have a widened nasal bridge, short philtrum, low-set and posteriorly rotated ears, and ocular hypertelorism. They are also at risk for progressive loss of hearing and therefore should have their hearing screened annually. Speech impairments are common and typically due to palatal abnormalities including:

- high arched palate,
- cleft palate,
- submucosal cleft,
- velopharyngeal incompetence, and
- a bifid uvula.

Dysfunction of the vocal cord(s) may also result from chronic intubation or injury to the recurrent laryngeal nerve during surgery. Dysfunction of the vocal cord(s) may lead to intermittent or chronic difficulties with speech or swallowing.

The most common endocrine disorders in patients with conotruncal lesions are related to thymic and parathyroid gland hypoplasia with DiGeorge syndrome. Neonates typically present with hypocalcaemia and hyperphosphataemia and may require supplements of calcium. As children grow, the remaining parathyroid tissue undergoes compensatory hyperplasia, and many older children and adults will have normal levels of calcium in later life.[4–7] These patients may also have deficiency of growth hormone and have short stature and failure to thrive. Autoimmune disease is also common in patients with DiGeorge syndrome, such as atopy, thyroid dysfunction, arthritis, or cytopenias.[4–7] In addition, thymic hypoplasia can predispose to immune dysfunction. T-cell deficiency and dysfunction can be noted in patients with DiGeorge syndrome. The T-cell deficits typically improve

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with age.[4–7] In addition, humoral deficits in B-cells are also present and typically cause deficiency of Immunoglobulin A and functional antibody defects to particular antigens (vaccinations).[4–7] All patients with DiGeorge syndrome should be followed by an immunologist. As they age, adults with DiGeorge syndrome require lifelong assessment of their thyroid gland and calcium homoeostasis, as well as their T- and B-cell function.

Pulmonary disease is also common in patients with conotruncal lesions and may consist of

- chronic lung disease,
- reactive airway disease,
- thromboembolic disease,
- restrictive pulmonary disease due to musculoskeletal or chest wall deformities such as scoliosis or medication administration (amiodarone), or
- pulmonary hypertension due to prior intracardiac shunts, abnormal pulmonary artery anatomy, pulmonary venous abnormalities, or left heart disease.

Premature infants and children with in uterine growth restriction will also have relative lung hypoplasia and be at risk for the development of pulmonary hypertension. Pulmonary hypertension can develop in anyone with congenital cardiac disease, especially if there is

- considerable pulmonary artery dysplasia,
- competitive flow to the lungs from collateral vessels,
- thromboembolic disease,
- right ventricular volume load (intracardiac shunt, tricuspid regurgitation, or pulmonary insufficiency),
- left heart disease, or
- delayed repair of an intracardiac shunt.[14]

Renal dysfunction may occur because of

- congenital renal anomalies,
- intrinsic disease of the kidney,
- systemic vascular issues,
- systemic hypertension, or
- multiple hypoxic episodes during cardiopulmonary bypass.

Congenital renal anomalies are commonly found in patients with congenital cardiac disease. Renal dysfunction is commonly found in adults with tetralogy of Fallot and proteinuria is common in patients with common arterial trunk.[15,16] All practitioners caring for adults with conotruncal congenital cardiac disease should have knowledge of prior renal ultrasounds or associated renal anomalies from alternative imaging modalities such as computerised tomographic imaging and magnetic resonance imaging.

Haematological abnormalities may also predispose to a hypercoaguable state and risk of thromboembolic disease. A family history of a hypercoaguable state should be excluded. A thorough review of the prior surgeries and cardiac catheterisations for any post-operative vascular complications is helpful before evaluating a new patient with congenital cardiac disease. Practitioners should also be aware of residual intracardiac shunts in patients with hypercoaguable states because of the potential risk of paradoxical embolic events. Vascular patency should also be assessed by ultrasound or alternative imaging modality before consideration of cardiac interventional procedures or cardiac surgical re-intervention. Consultation with Haematology should be utilised when clinically indicated.

The extracardiac anomalies associated with conotruncal congenital cardiac disease requires a multidisciplinary team approach to the long-term care of these patients. As described above, the multidisciplinary team may include the following members:

- genetics,
- developmental paediatrics,
- neurology,
- psychiatry,
- speech therapy,
- occupational and physical therapy,
- audiology,
- otolaryngology (Ear, Nose, and Throat surgeons),
- immunology,
- endocrinology,
- pulmonology,
- nephrology, and
- haematology.

Acquired cardiovascular disease

Pregnancy is usually well tolerated in women with conotruncal congenital cardiac disease. Counselling before conception should occur in all women and adolescents of child-bearing age and should include:

- discussion on birth control,
- risk of thromboembolic events,
- arrhythmias,
- residual valvar stenosis and/or regurgitation,
- ventricular function, and
- risk of recurrence of congenital cardiac disease.

All patients should have coordinated care involving obstetrics, maternal–foetal medicine, and cardiology throughout the pregnancy in order to maximise the outcome for the foetus and the mother. Low-risk pregnancies include:

- residual intracardiac shunts, and
- mild to moderate pulmonary stenosis or valvar regurgitation with normal systolic function.

https://doi.org/10.1017/S104795111200203X Published online by Cambridge University Press

Intermediate risk pregnancies include:

- unrepaired or palliated cyanotic congenital heart disease,
- coarctation of the aorta,
- mild or moderate aortic stenosis,
- presence of a mechanical prosthetic valve,
- severe pulmonary stenosis,
- moderate or severe ventricular dysfunction, and
- symptomatic arrhythmias.

High-risk pregnancies or contraindications to pregnancy include:

- New York Heart Association functional Class 3 or 4,
- significant pulmonary hypertension,
- Marfan syndrome with significant aortic root dilation or valvar involvement, and
- severe aortic stenosis.

Patients with tetralogy of Fallot, common arterial trunk, and transposition of the great arteries usually tolerate pregnancy well; however, high-risk obstetrical care and delivery should be coordinated through their cardiologist and maternal–foetal medicine specialist to maximise the outcomes for both the mother and the foetus.[17]

Endocarditis may potentially occur in any patient with unrepaired or palliated congenital cardiac disease. It typically presents in areas where there is turbulent flow of blood, which injures the endocardium and creates a nidus for bacterial growth. Endocarditis usually presents on the atrial side of atrioventricular valves or ventricular side of semilunar valves. The definition of infective endocarditis is two major criteria; one major and three minor criteria, or five minor criteria based on the modified Duke criteria. Antibiotic prophylaxis is required for all patients with:

- prosthetic heart valve,
- previous infective endocarditis,
- unrepaired cyanotic congenital cardiac disease,
- repaired congenital cardiac disease with prosthetic material or device for the first 6 months after the procedure,
- repaired congenital cardiac disease with a residual defect that inhibits endothelialisation, and
- cardiac transplantation.

As patients with conotruncal congenital cardiac disease age, they are at risk of developing obesity, hypertension, hyperlipidaemia, all of which may predispose to coronary artery disease and peripheral vascular disease. Atherosclerosis and the cardiovascular risk profile of patients with congenital cardiac disease has become a topic of recent interest. The need exists for more studies to investigate these profiles, and to provide policies for long-term care of the adults with congenital heart disease. In the United States, the National Heart, Lung, and Blood Institute Working Group on Obesity and Other Cardiovascular Risk Factors in Congenital Heart Disease released a report in 2010, which raised awareness of the existing gaps in knowledge and presented data from healthy children with potential applicability to children with congenital cardiac disease.[18] A significant percentage of children with congenital cardiac disease were also found to be obese or overweight according to recent studies.[19] Currently, little is known about how children with congenital cardiac disease will be affected by obesity. Patients with congenital cardiac disease have an abnormal myocardial substrate. Their abnormally formed myocardium, having been exposed to periods of cyanosis, and later, to ischaemia–reperfusion injury during open heart surgery, makes for an abnormal substrate. This abnormal substrate puts them at risk for developing ventricular dysfunction, arrhythmias, and cardiac failure, which makes them especially vulnerable to potentially superimposed long-term cardiovascular risk factors. Obesity is a risk factor for developing hypertension, insulin resistance, and dyslipidaemia. In addition, increased inflammatory cytokines, sleep apnoea, autonomic imbalance, and abnormal cardiac remodelling are known to occur with obesity.[20] Hypertension in obese individuals is caused by a combination of fluid retention and increased cardiac output.[21,22] Resistance to insulin results in altered metabolism of lipids resulting in

- unfavourable and atherogenic lipid patterns,
- altered vascular reactivity in both peripheral and coronary arterial beds,
- non-alcoholic fatty liver, and
- the development of type 2 diabetes mellitus.

Increases in the circulating inflammatory cytokines in obese individuals are also related to atherosclerosis and coronary artery disease.[23–27] The autonomic imbalance consisting of a pattern of sympathetic predominance results in a reduction in variability of the rate of the heart and predisposes individuals to atrial and ventricular dysrhythmias.[28,29] Studies have also demonstrated a link between obesity and diastolic and systolic ventricular dysfunction, left ventricular hypertrophy, and congestive cardiac failure.[30,31] Cardiovascular risk probably varies by type of lesion. Lesions that have developmental anomalies of the coronary arteries or surgically manipulated coronary arteries, as well as left-sided obstructive lesions, may be at higher risk.[32] Cyanotic lesions appear to be protective

https://doi.org/10.1017/S104795111200203X Published online by Cambridge University Press

against coronary artery disease.[33,34] All practitioners, especially paediatric cardiologists who care for adults with congenital cardiac disease, must be aware of the potential for adults with congenital cardiac disease to develop traditional acquired adult cardiovascular disease.

Conclusion

As our patients with conotruncal congenital cardiac disease live into adulthood, we are learning more about the complications of long-term life. Multi-disciplinary care teams are needed and include experts in

- paediatric cardiology,
- adult cardiology,
- advanced cardiac imaging including computed tomography and magnetic resonance imaging,
- electrophysiology,
- interventional cardiology,
- cardiothoracic surgery, and
- subspecialist care that includes genetics, immunology, endocrinology, nephrology, haematology, neurology, developmental specialists, psychiatry, obstetrics, and maternal–foetal medicine.

Routine surveillance with comprehensive screening for structural heart disease, functional heart disease, thromboembolic disease, arrhythmias, associated end-organ dysfunction, and acquired cardiovascular disease is important. Future research will better define the care plans for routine surveillance in these patients.

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https://doi.org/10.1017/S104795111200203X Published online by Cambridge University Press