

Review Article

Cardiac care of children with common genetic syndromes: a practical review for pediatricians and pediatric cardiologists

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Received: 20 May 2026

Accepted: 04 June 2026

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ABSTRACT

Genetic syndromes are an important consideration in pediatric cardiac care because the specific syndrome can influence the likelihood of particular cardiac anomalies, timing and nature of cardiac evaluation, imaging modality, pulmonary hypertension risk, anesthesia planning, and intensity of subsequent surveillance. This review covers the evaluation and management of children with Down syndrome, 22q11.2 deletion syndrome, Turner syndrome, Noonan syndrome and related RASopathies, Williams syndrome, Marfan syndrome and Loeys-Dietz syndrome, Duchenne muscular dystrophy, and several less common genetic syndromes of high yield. Each section focuses on clinical and epidemiologic features, typical entry points into cardiac evaluation, timing of evaluation, minimum cardiac evaluation, stabilization or disposition tier, management modifiers, and criteria for escalation of care. A practical principle that guides this review is that the cardiac findings define acuity, whereas the genetic findings define what to look for, how long to follow the child, and whether normal baseline imaging ends surveillance. Newborn echocardiography is indicated in children with Down syndrome; conotruncal or arch anomalies should prompt consideration of 22q11.2 deletion syndrome; Turner syndrome requires lifelong aortic and blood pressure surveillance; Williams syndrome requires arteriopathy and anesthesia-risk assessment; and Duchenne muscular dystrophy requires presymptomatic cardiomyopathy surveillance.

Keywords: Pediatric cardiology, Congenital heart disease, Genetic syndromes, Echocardiography, Aortopathy, Cardiomyopathy

INTRODUCTION

In children with genetic syndromes, pediatric cardiology evaluation is typically predictable. Children can be identified prenatally for cardiac and/or genetic anomalies, in the newborn period because of murmur, cyanosis, failed critical congenital heart disease screening, or later because of hypertension, aortopathy, cardiomyopathy, arrhythmias, decreased exercise ability, syncope, or preoperative clearance.^{1,2} A syndrome-based review is clinically useful because the pediatrician or cardiologist often starts from a suspected or confirmed genetic diagnosis and needs a timeline: when to obtain echocardiograms or electrocardiograms, when to use

cross-sectional imaging, what to do with an abnormal finding, and whether normal baseline imaging ends surveillance. The review is organized by eight clinical syndrome sections.

Each section translates the genetic diagnosis into a cardiac care pathway, including timing of testing, cross-sectional imaging, findings that require urgent work-up, and findings that do not end surveillance.

GENERAL CARDIAC-CARE FRAMEWORK

Assess entry trigger, acuity of presentation, minimum workup required, risk to patient, appropriate care tier and

next measurable output. Newborns with suspicion of arch obstruction, left-sided obstruction, hypertension, or arteriopathy require assessment of preductal and

postductal oxygen saturation, pulse quality and perfusion, assessment of respiratory effort and feeding and assessment of blood pressure in all four extremities.^{1,2}

Table 1: Syndrome-specific cardiac-care timing and surveillance.

Syndrome	Dominant cardiac phenotype	Initial evaluation timing	Surveillance timing	Key escalation triggers
Down syndrome	AVSD, VSD, ASD, PDA, pulmonary hypertension risk	Fetal ECHO at 18-22 weeks if suspected prenatally; postnatal ECHO for every infant regardless of fetal ECHO	Lesion-driven after ECHO; AVSD physiology reassessed during first month and 1-3 months; repaired lesions followed by residual findings	Poor growth, tachypnea, AV valve regurgitation, rising RV pressure, PH, residual shunt, LVOT obstruction
22q11.2 deletion	Conotruncal and arch disease: TOF, truncus, IAA-B, PA/VSD, arch anomalies	Fetal ECHO and CMA/22q11 testing when conotruncal/arch lesion detected; newborn ECHO and prostaglandin pathway if ductal-dependent	Lesion-dependent; adult congenital transition for repaired TOF/truncus/conduit/arch disease	Cyanosis, arch obstruction, RVOT obstruction, hypocalcemia, immune risk, feeding/airway issues, postoperative conduit/PA disease
Turner syndrome	BAV, coarctation, arch disease, hypertension, aortic dilation	ECHO and ECG at diagnosis; four-limb BP/pulses when obstruction suspected	Repeat imaging around 9-11 years, after growth completion/transition, and every 5-10 years lifelong when stable	Hypertension, BP gradient, weak femoral pulses, aortic growth, BAV dysfunction, pregnancy planning
Noonan/RASopathies	Dysplastic pulmonary valve stenosis, HCM, ASD, branch PA stenosis	ECHO and ECG at diagnosis; fetal ECHO for NT, hydrops, pulmonary stenosis or fetal HCM	Annual cardiac evaluation until age 5 if baseline normal; at least every 5 years after age 5/adulthood or more often if disease present	Rising gradient, progressive HCM, outflow obstruction, arrhythmia, poor growth, procedural bleeding risk
Williams syndrome	SVAS, branch PA stenosis, hypertension, coronary/systemic arteriopathy	ECHO, ECG, four-limb BP and pulses at diagnosis; CTA/MRA when ECHO cannot define arterial/coronary risk	Severity-driven by gradients, BP, ventricular hypertrophy, symptoms, and procedure plans	Syncope, chest pain, ischemic ECG, rising SVAS/PA gradient, hypertension, planned sedation/anesthesia
Marfan/LDS	Aortic root/systemic aneurysm, valve disease, arterial tortuosity	ECHO at diagnosis; LDS also baseline head-to-pelvis CTA/MRA	Marfan: repeat ECHO about 6 months then often annually if stable; LDS interval by genotype/vessel size/growth	Aortic growth, elevated Z-score/index, family dissection history, symptoms, pregnancy/transition, systemic aneurysm
Duchenne muscular dystrophy	Progressive cardiomyopathy, fibrosis, arrhythmia	Cardiology evaluation at diagnosis with ECG and imaging; CMR when feasible	At least annual surveillance even when EF is normal	Fibrosis, LV dysfunction/dilation, arrhythmia, surgery/anesthesia planning, respiratory decline

Continued.

Syndrome	Dominant cardiac phenotype	Initial evaluation timing	Surveillance timing	Key escalation triggers
Selected high-yield pathways	MPS valve/cardiomyopathy; Holt-Oram conduction; TSC rhabdomyoma; EVC AV canal/common atrium; Alagille branch PA; CHARGE conotruncal/arch; Kabuki left-sided obstruction	Baseline ECHO/ECG or fetal ECHO depending syndrome and presentation	Syndrome- and lesion-driven; TSC rhabdomyoma ECHO every 1-3 years until regression; MPS serial ECHO/ECG based on type and findings	Valve progression, AV block/syncope, tumor obstruction/arrhythmia, PH, liver/coagulation risk, airway/feeding risk, coarctation signs

ASD: atrial septal defect; AV: atrioventricular; AVSD: atrioventricular septal defect, BAV: bicuspid aortic valve, BP: blood pressure, CHD: congenital heart disease, CMA: chromosomal microarray, CMR: cardiac magnetic resonance imaging, CTA: computed tomography angiography, DMD: Duchenne muscular dystrophy, ECG: electrocardiography, EF: ejection fraction, EVC: Ellis-van Creveld, HCM: hypertrophic cardiomyopathy, IAA-B: interrupted aortic arch type B, LDS: Loeys-Dietz syndrome, LV: left ventricle, LVOT: left ventricular outflow tract, MPS: mucopolysaccharidoses, MRA: magnetic resonance angiography, NT: nuchal translucency, PA: pulmonary artery, PDA: patent ductus arteriosus, PH: pulmonary hypertension, RV: right ventricle, RVOT: right ventricular outflow tract, SVAS: supravalvar aortic stenosis, TOF: tetralogy of Fallot, TSC: tuberous sclerosis complex, VSD: ventricular septal defect.

Table 2: Cross-syndrome escalation triggers and clinical actions.

Trigger/finding	Interpretation	Main syndromes	Action/output
Cyanosis, failed CCHD screen, shock, weak pulses	Possible ductal-dependent systemic/pulmonary blood flow or critical obstruction	22q11.2 deletion, Turner, CHARGE, complex CHD	Same-day ECHO, ECG, pre/post ductal SPO ₂ , four-limb BP, prostaglandin consideration, cardiac-center transfer
Poor feeding, tachypnea, diaphoresis, poor growth	Pulmonary over circulation or heart failure physiology	Down syndrome, Ellis-van Creveld, large shunt lesions	Reassess shunt, AV valve regurgitation, RV pressure and nutrition; start/adjust diuretics if congestive; discuss earlier repair
Rising outflow or branch pulmonary artery gradient	Progressive obstruction or multilevel stenosis	Noonan/RASopathies, Williams, Alagille	Shorten ECHO interval, use CTA/MRA/CATH if anatomy unclear, refer for catheter/surgical review
Hypertension or arm-leg BP gradient	Coarctation, arch disease, renal/diffuse arteriopathy, or aortic risk	Turner, Williams, Kabuki	Four-limb BP, ambulatory BP if needed, arch/arterial imaging, treat BP and reassess aortic risk
Aortic growth or high Z-score/index	Progressive aortopathy	Turner, Marfan, Loeys-Dietz	Shorten imaging interval, optimize beta-blocker/ARB, exercise guidance, aortic-center referral, pregnancy counseling when relevant
Fibrosis or ventricular dysfunction	Subclinical or progressive cardiomyopathy	DMD, RASopathies, MPS	Start/intensify cardiomyopathy therapy, repeat CMR/ECHO, rhythm monitoring, perioperative risk update
Syncope, AV block, bradycardia, arrhythmia	Conduction disease or malignant rhythm risk	Holt-Oram, MPS, Williams, repaired CHD	ECG, Holter/event monitor, electrophysiology referral, pacemaker/therapy evaluation when indicated
Planned sedation, catheterization or surgery	Unrecognized coronary, airway, PH, cardiomyopathy, or aortopathy risk	Williams, MPS, DMD, LDS, severe PH, 22q11.2 deletion	Update cardiac assessment; coordinate cardiac anesthesia or appropriate center; correct calcium/coagulation/respiratory risks when relevant

ARB: angiotensin receptor blocker, AV: atrioventricular, BP: blood pressure, CCHD: critical congenital heart disease, CHD: congenital heart disease, CMR: cardiac magnetic resonance imaging, CTA: computed tomography angiography, DMD: Duchenne muscular dystrophy, ECG: electrocardiography, LDS: Loeys-Dietz syndrome, MPS: mucopolysaccharidoses, MRA: magnetic resonance angiography, PH: pulmonary hypertension, RV: right ventricle, SpO₂: oxygen saturation.

For every child with suspected or confirmed congenital heart disease, transthoracic echocardiography establishes

the diagnosis and determines cardiovascular impact, including ventricular function, pulmonary artery pressure

estimate, ductal dependence, valve disease, and postoperative residual lesions. Depending on findings, ECG, Holter monitoring, cardiac magnetic resonance imaging, computed tomography angiography, magnetic resonance angiography, or catheterization may be indicated.^{1,2} Next, the intended level of care must be stated. Tier 0 includes critically ill patients requiring same-day critical care and cardiology management.

Tier 1 is screening only when evaluation is normal and no progressive syndrome-driven risk exists. Tier 2 is lesion-based follow-up. Tier 3 is syndrome-driven longitudinal surveillance despite normal baseline imaging. Tier 4 includes aortopathy, coronary risk, hypertrophic cardiomyopathy, pulmonary hypertension, cardiomyopathy or increased anesthesia risk requiring multimodality or procedure-specific planning. These clinical situations are summarized in Table 1 and 2.

Down syndrome

Down syndrome, or trisomy 21, affects approximately 1 in 640 to 700 live births. Approximately 40%-50% of affected children are born with congenital heart disease. Atrioventricular septal defects are the most common lesions, followed by ventricular septal defects, atrial septal defects, patent ductus arteriosus and rarely tetralogy of Fallot or other complex lesions. Many defects create large left-to-right shunts, pulmonary overcirculation, atrioventricular valve regurgitation, growth difficulty and pulmonary hypertension risk.³⁻⁵

Prenatal diagnosis of heart defects in a fetus suspected of having Down syndrome is identified by aneuploidy screening, increased nuchal translucency, fetal anomaly scan, or suspected atrioventricular septal defect. Fetal echocardiography is typically performed at 18 to 22 weeks' gestation and assesses atrioventricular septation, ventricular size and function, atrioventricular valve regurgitation, outflow tracts, great arteries, aortic arch, fetal heart rate, and fetal heart failure. Earlier fetal echocardiograms can be performed in high-risk pregnancy but require second-trimester confirmation if incomplete.^{2,3}

Echocardiograms for the newborn with Down syndrome should be completed in the newborn period regardless of whether fetal echocardiography was performed or appeared reassuring. Initial assessment includes preductal and postductal oxygen saturation; pulse and perfusion assessment; respiratory and feeding status; hepatomegaly; shunt size; atrioventricular valve regurgitation; ventricular balance; patent ductus arteriosus; arch anatomy; and right ventricular pressure estimate. Same-day cardiology evaluation is required for cyanosis, failed pulse oximetry screening, respiratory distress, shock, abnormal differential saturations, poor pulse strength or major structural congenital heart defects.³

The cardiologist monitors the child as pulmonary vascular resistance drops. In the first month, cardiac anatomy and baseline physiology are confirmed. Between one and three months, the cardiologist evaluates pulmonary overcirculation, heart failure, nutrition, diuretic need and need for early surgical correction. Balanced complete atrioventricular septal defect is typically repaired between 3 and 6 months of life, earlier when poor growth, severe pulmonary overcirculation, atrioventricular valve regurgitation, or pulmonary hypertension develops.^{4,5}

Follow-up of postoperative congenital heart disease in the child with Down syndrome is residual-lesion based. After complete atrioventricular septal defect repair, follow-up evaluates residual left atrioventricular valve regurgitation, left ventricular outflow tract obstruction, residual shunt, ventricular dysfunction and abnormal rhythm. Airway obstruction, aspiration, chronic lung disease, and sleep-disordered breathing can worsen pulmonary hypertension; polysomnography is recommended by 3 to 4 years of age or earlier when symptoms or pulmonary hypertension are present.^{3,4}

22q11.2 deletion syndrome

22q11.2 deletion syndrome is the most common recurrent microdeletion and has an estimated frequency of approximately 1 in 4,000 live births, with congenital heart disease reported in a large proportion of affected individuals. Frequent heart defects are conotruncal and aortic arch defects, including tetralogy of Fallot, truncus arteriosus, interrupted aortic arch type B, pulmonary atresia with ventricular septal defect, conoventricular ventricular septal defect, right-sided aortic arch and vascular rings.^{6,7} Prenatal diagnosis usually follows fetal echocardiographic recognition of a conotruncal or arch anomaly, after which fetal cardiology determines ductal dependence, need for prostaglandin E1 and delivery site.^{2,6,7}

Assessment of cardiac findings and their impact on the fetus is critical. Detailed intracardiac and great vessel assessment should define arch sidedness and branching, ductal dependence, branch pulmonary arteries and vascular rings. Newborns with interrupted aortic arch, severe pulmonary blood flow obstruction, severe cyanosis, shock or severe ductal dependence may require prostaglandin E1 and intensive care with cardiac surgical capability before urgent surgical or catheter-based planning. Noncritical ventricular septal defects and tetralogy of Fallot require pediatric cardiology follow-up based on right ventricular outflow obstruction, pulmonary artery growth and arch sidedness.

Several medical problems common in 22q11.2 deletion syndrome can affect cardiac surgery. Hypocalcemia can be associated with seizures, arrhythmias, and perioperative instability. Immune dysfunction can affect infection and transfusion planning. Airway, palate, and

feeding difficulties can affect extubation, aspiration risk, and preoperative growth. The genetics information therefore becomes important preoperative information for the cardiac center.^{6,7} Escalation triggers include cyanosis, increased right ventricular outflow tract obstruction, arch obstruction, differences in pulses and blood pressure, poor growth, recurrent aspiration or failure to thrive, preoperative hypocalcemia, immune dysfunction, postoperative pulmonary regurgitation, branch pulmonary artery stenosis, conduit problems, residual ventricular septal defect, arrhythmias and right ventricular dilatation. Repaired tetralogy of Fallot, truncus arteriosus, conduit repairs, arch repairs and pulmonary artery repairs require transition to adult congenital heart disease care.

Turner syndrome

Turner syndrome affects approximately 1 in 2,000 to 2,500 live-born female infants, and the major cardiovascular concern is left-sided obstruction and aortopathy. Approximately 15%-30% have bicuspid aortic valve, 7%-18% have coarctation of the aorta and many develop aortic dilation or systemic hypertension. The risk domain therefore includes aortic, arch, valve, and blood pressure risk, not only childhood screening for coarctation.⁸

Prenatal risk factors for Turner syndrome include cystic hygroma, fetal hydrops, fetal edema, left-sided heart obstruction, and/or suspected coarctation of the aorta. Fetal echocardiography can evaluate for left-sided heart obstructive lesions including suspected coarctation of the aorta, evaluate cardiac chamber enlargement, measure aortic valve and aortic arch dimensions and help determine the cardiac contribution to fetal hydrops. Even a normal fetal echocardiogram does not rule out coarctation of the aorta and a high degree of suspicion is required in the postnatal period because the ductus arteriosus can mask the degree of arch obstruction.^{2,8}

Children with Turner syndrome should have a complete cardiovascular evaluation at diagnosis even if prenatal and newborn cardiovascular evaluations appeared normal. Echocardiography and ECG are minimum evaluation, with four-limb blood pressure when possible, femoral pulse assessment, blood pressure classification, and assessment for bicuspid aortic valve, coarctation, arch anomalies, partial anomalous pulmonary venous connection, aortic dilation, and ventricular dysfunction. Suspected neonatal coarctation requires follow-up after ductal closure.⁸ Children with Turner syndrome should have their first cardiology evaluation at the time of diagnosis, followed by studies in later childhood around age 9 to 11 years and at completion of growth. Individuals with no known cardiac defects require cardiac evaluation and monitoring at transition to adult healthcare and then every 5 to 10 years thereafter when stable. Cardiac magnetic resonance imaging is recommended when feasible because it can better outline the aortic arch and thoracic aorta than echocardiography. Patients with

Turner syndrome should have blood pressure actively monitored and should be considered for ambulatory blood pressure monitoring if clinical blood pressure measurements are abnormal.⁸ Children with Turner syndrome need increased surveillance when they have weak femoral pulses, an upper-to-lower extremity blood pressure difference, hypertension, bicuspid aortic valve with stenosis or regurgitation, coarctation of the aorta, increasing aortic size with an increasing aortic size index, chest pain, or shortness of breath with exercise. Increased surveillance is also needed when the aortic arch and thoracic aorta cannot be fully visualized using two-dimensional echocardiography and when adolescents or adults are planning pregnancy or fertility treatment.⁸

Noonan syndrome and related RASopathies

The RASopathies are a group of conditions affecting the RAS-MAPK pathway. Approximately 50%-80% of individuals with a RASopathy will have some form of congenital heart disease, with pulmonary valve stenosis found in approximately 25%-70% of individuals and often dysplastic in nature. Hypertrophic cardiomyopathy is less common in most RASopathies but is considered particularly high risk in individuals with Noonan syndrome and related disorders. Other heart problems can also occur, including atrial septal defects and branch pulmonary artery stenosis.^{9,10} Prenatal findings are reported to occur in approximately 20%-50% of children with RASopathies and may include increased nuchal translucency, cystic hygroma, hydrops, or polyhydramnios. Increased fetal cardiac size, fetal pulmonary stenosis or severe fetal hypertrophic cardiomyopathy is also reported in RASopathies.

Prenatal and postnatal echocardiography are critical for determining pulmonary valve morphology, degree of stenosis, ventricular wall thickness and function, and presence of arrhythmias. A fetus with severe hypertrophic cardiomyopathy or hydrops requires serial fetal echocardiography and preparation for delivery and intensive care of a neonate with severe cardiomyopathy, potential early life-threatening arrhythmias, or respiratory compromise.^{2,9,10}

The postnatal evaluation of cardiac function in children with Noonan syndrome typically involves echocardiography and ECG. Children with normal cardiac findings who are evaluated for Noonan syndrome before 5 years of age should have periodic evaluations annually until 5 years of age and then at least every 5 years thereafter through adulthood. Children with cardiac findings require lesion-specific follow-up rather than a fixed 5-year interval.^{9,10} In children with RASopathies, management should be individualized based on the characteristics of the pulmonary valve, degree of myocardial involvement and bleeding risk. Children with severe pulmonary stenosis and dysplastic pulmonary valves are generally more challenging to manage with balloon valvuloplasty than children with stenotic, doming

pulmonary valves and may require consideration of a surgical approach. Children with hypertrophic cardiomyopathy require increased frequency of imaging and rhythm monitoring as wall thickness and degree of outflow obstruction increase or left ventricular function deteriorates. In children with RASopathies and a history of bleeding, bleeding diathesis must be considered prior to catheterization and/or surgery with coagulation studies reviewed in detail.^{9,10}

Triggers for increasing frequency of imaging, intervention, or RASopathy testing include worsening pulmonary stenosis and associated symptoms such as cyanosis or exercise intolerance; increasing ventricular wall thickness; worsening outflow obstruction; decreased ventricular function; clinical concern for arrhythmias; and decreased growth and feeding in infants. Children with isolated pulmonary stenosis or hypertrophic cardiomyopathy should be considered for RASopathy testing especially when features of RASopathies are present in the patient or a first-degree relative, such as short stature, pectus, lymphatic issues, undescended testes, characteristic facial features or other RASopathy features.^{9,10}

Williams syndrome

Williams syndrome is a 7q11.23 microdeletion syndrome caused by elastin haploinsufficiency. The diffuse arteriopathy of vessels of different sizes is the hallmark of the condition and cardiovascular anomalies are present in approximately 80% of individuals with Williams syndrome. Supravalvar aortic stenosis and peripheral or branch pulmonary artery stenosis are the most common anomalies and are often associated with increased blood pressure. Other associated features include coronary artery ostial involvement, renal artery stenosis, increased ventricular mass, and other arterial stenoses. Williams syndrome is therefore characterized by generalized systemic arteriopathy with significant implications for the coronary arteries and anesthesia.¹¹⁻¹³

Children with Williams syndrome are typically diagnosed in the neonatal period or later in childhood and are often referred for murmur, supravalvar aortic stenosis, peripheral or branch pulmonary artery stenosis, hypertension, failure to thrive, irritability or hypercalcemia. Four-limb blood pressure, pulse examination, ECG and echocardiography should define supravalvar aortic stenosis gradient, pulmonary artery stenosis, ventricular hypertrophy, ventricular function, and visible coronary artery origins. If echocardiography cannot define the arterial tree, branch pulmonary arteries, renal arteries or coronary arteries, computed tomography angiography or magnetic resonance angiography is required.¹¹⁻¹³ Monitoring for Williams syndrome is severity-based. A child with mild peripheral pulmonary artery stenosis may improve over time, whereas children with supravalvar aortic stenosis, diffuse aortic stenosis, coronary disease concern, biventricular outflow

obstruction, or hypertension need more frequent monitoring for changes in gradient, degree of ventricular hypertrophy, development of new symptoms and need for intervention. Hypertension needs evaluation for renal artery stenosis or diffuse arterial stenosis rather than management as essential hypertension alone.¹¹⁻¹³

Procedural risk for sedation, catheterization and surgery is increased in children with Williams syndrome and severe cardiac anomalies. A current cardiac evaluation before elective sedation or anesthesia is indicated to assess gradients, blood pressure for age and height, degree of ventricular hypertrophy and extent of coronary artery involvement. Decisions regarding need for cardiac anesthesia and for cardiac versus non-cardiac center location should be made with these anomalies in mind.¹⁴ The child with increasing supravalvar or pulmonary artery gradients, chest pain, syncope, ischemic ECG changes, increased left ventricular mass, hypertension or coronary disease should have cardiac evaluation intensified before sedation or anesthesia. The degree of supravalvar aortic stenosis, pulmonary artery stenosis, and prior cardiac findings guides the required preoperative evaluation. This should not be a blanket clearance statement; it should be an anatomy-based assessment of procedural risk.

Marfan syndrome and Loeys-Dietz syndrome

Two heritable conditions that can cause problems with the thoracic aorta in children and adolescents are Marfan syndrome and Loeys-Dietz syndrome. The pediatric cardiac center's focus in managing children with these heritable conditions of the aorta is to make an early diagnosis of aortic disease and then measure the aorta over time, treat the child medically, counsel regarding level of exercise, screen family members and refer to an aortic center when aortic size, growth rate, symptoms, genotype or family history meets referral thresholds.¹⁵⁻¹⁸ Both Marfan syndrome and Loeys-Dietz syndrome can enter cardiology through family history of thoracic aortic disease or subtle clinical features. Echocardiography measures the aorta at specific points and assesses the aortic valve using pediatric z-scores. For Marfan syndrome, echocardiography is performed at diagnosis and repeated approximately 6 months later to assess growth; stable patients typically undergo annual echocardiography, while enlarged or rapidly growing aortas require more frequent studies. Loeys-Dietz syndrome requires broader first workup because arteries outside the aortic root can be involved; baseline magnetic resonance angiography or computed tomography angiography from head to pelvis defines aneurysms, arterial tortuosity, branch-vessel disease, and distal arterial disease.¹⁵⁻¹⁸ The main goals of treatment for children with thoracic aortic disease are monitoring for dissection risk, medical therapy, exercise counseling, family screening and surgical referral when needed. Beta-blockers and/or angiotensin receptor blockers are commonly used, individualized by aortic size, growth

rate, blood pressure, genotype and tolerance. Children with smaller stable aortas can generally engage in low to moderate dynamic exercise, while those with larger or rapidly growing aortas are generally restricted from high-static, high-impact and isometric exercise.¹⁵⁻¹⁸

Escalation should be considered for aortic growth, high or increasing aortic z-score, or new significant valvular disease. Before transition, the child and family should have an identified adult aortopathy center and a plan for heritable thoracic aortic disease testing of relatives when indicated by the child's genetics.¹⁵⁻¹⁸

Duchenne muscular dystrophy

Duchenne muscular dystrophy is an X-linked disorder affecting approximately 1 in 3,500 to 5,000 live male births. The cardiac manifestation of Duchenne muscular dystrophy is not a typical congenital heart defect, but rather a progressive dystrophin-deficient cardiomyopathy that can be associated with progressive and potentially fatal myocardial fibrosis. The clinical course is generally indolent with onset of left ventricular dysfunction with or without ventricular chamber dilatation, followed by risk of life-threatening arrhythmias and heart failure, which may be clinically silent in less mobile individuals because of decreased activity.^{19,20}

The cardiac effects of Duchenne muscular dystrophy should be assessed at the time of initial diagnosis for the muscular disorder. Evaluation includes ECG and assessment of the heart by echocardiography and/or cardiac magnetic resonance imaging. Although cardiac magnetic resonance imaging may be normal in a clinically well child with Duchenne muscular dystrophy and normal echocardiography, it can identify decreased left ventricular function and late gadolinium enhancement in the myocardium. Thus, even in children with Duchenne muscular dystrophy and normal echocardiography, annual evaluation by a cardiologist is indicated.^{19,20}

Prevention is time-based and finding-based. Initiation of an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker is recommended around the age of 10 years; however, in the presence of left ventricular dysfunction, ventricular chamber enlargement, evidence of myocardial fibrosis, or other myocardial abnormality on imaging, this should be started earlier. Other heart failure medications can be added as needed based on left ventricular function, degree of myocardial fibrosis, cardiac rhythm, blood pressure, and clinical status of heart failure.^{19,20} A disease-specific modifier in Duchenne muscular dystrophy is the combination of progressing cardiomyopathy, deteriorating respiratory function, corticosteroid exposure, scoliosis surgery, loss of ambulation and anesthesia risk. Thus, before any major orthopedic, respiratory or other surgery, the cardiac assessment should be up to date, including left ventricular function,

cardiac rhythm, cardiac medications, respiratory support and anesthesia-related risk. An outdated normal echocardiogram is not sufficient for a safe surgical plan.

Indications for intensification of heart failure treatment include myocardial fibrosis on cardiac magnetic resonance imaging, declining ejection fraction, increasing left ventricular end-diastolic volume, tachyarrhythmias, conduction disturbances, heart failure symptoms, noninvasive ventilation, surgery, or sedation need. Children with Duchenne muscular dystrophy should transition to adult neuromuscular-cardiology providers; waiting for exertional fatigue delays important treatment.

Selected less common but high-yield syndromic cardiac pathways

The mucopolysaccharidoses cause progressive cardiac disease with thickened valves causing regurgitation or stenosis, increased ventricular mass, dilated cardiomyopathy, coronary artery disease, conduction disease, or pulmonary hypertension. Diagnosis should prompt echocardiography and ECG, followed by serial follow-up based on mucopolysaccharidosis type, age, findings, and planned anesthesia. The child's airway, cervical spine, chest and cardiac condition affect sedation or surgery and require pre-procedural cardiology and anesthesiology planning.^{21,22}

Various conditions can be associated with congenital heart disease and conduction defects. Children with Holt-Oram syndrome have cardiac and conduction abnormalities associated with upper extremity radial-ray malformations and atrial and ventricular septal defects. After surgical repair of congenital heart disease, children with Holt-Oram syndrome need continued follow-up for rhythm disturbances because conduction defects can progress after surgical correction. Children with Holt-Oram syndrome who experience syncope, PR interval prolongation, bradycardia, or other indications of conduction disturbance should have Holter monitoring and electrophysiology referral for further management.²³

Tuberous sclerosis complex is often diagnosed in cardiac consultations when fetal or infant rhabdomyomas are found. Rhabdomyomas can be obstructive, cause life-threatening arrhythmias, or cause heart failure and hydrops. Prenatal evaluation of a fetus with suspected tuberous sclerosis complex or fetal cardiac tumors should include fetal echocardiography. Children with rhabdomyomas typically undergo echocardiography every 1 to 3 years until regression, while symptomatic, obstructive or arrhythmogenic tumors require more frequent pediatric cardiology follow-up or inpatient management.^{24,25} Children with Ellis-van Creveld syndrome can have atrial-level septation defects, common atrium, atrioventricular canal-type defects, venous anomalies, and pulmonary hypertension risk. Echocardiography should assess atrial septation, atrioventricular valve anatomy, ventricular size and

function, systemic and pulmonary venous return, shunt size and right ventricular pressure. Growth and respiratory status are as critical as shunt size in determining timing of repair; a large shunt with severe thoracic restriction or respiratory compromise may require earlier intervention.²⁶

In Alagille syndrome, branch pulmonary artery stenosis, pulmonary valve stenosis or atresia, and tetralogy of Fallot-like malformations occur in a significant proportion of children. Echocardiography can assess right ventricular pressure, pulmonary valve stenosis and pulmonary artery size but branch pulmonary artery assessment can be challenging. Cross-sectional imaging or cardiac catheterization is frequently required to determine pulmonary artery size. Liver disease, cholestasis, coagulopathy, portal hypertension and liver transplant status affect catheterization, surgery and anesthesia decisions.²⁷

Children with CHARGE syndrome, or CHD7 disorder, typically have conotruncal defects and/or arch anomalies. Echocardiograms should be performed at the time of diagnosis. Children with critical or highly complex cardiac defects identified prenatally should be delivered at a cardiac-capable center. The modifier for preoperative risk is perioperative physiology. Choanal atresia, airway anomalies, aspiration, feeding difficulties, and growth failure affect extubation, preoperative nutrition, and postoperative recovery for children with CHARGE syndrome.²⁸ A variety of cardiac anomalies are identified in children with Kabuki syndrome, most often left-sided obstruction such as coarctation of the aorta or bicuspid aortic valve with associated septal defects. Echocardiography should be performed as part of initial evaluation and should assess the aortic arch, aortic valve, septa, ventricles, functional status, and pulmonary pressure when indicated. Follow-up is recommended for coarctation, bicuspid aortic valve, left-sided obstruction or other cardiac defects. Children with normal echocardiograms and no cardiac symptoms may be discharged from intensive cardiac surveillance with referral for symptoms, murmur, hypertension, abnormal pulses, or concern for missed coarctation.^{29,30}

Cross-syndrome practical rules

A child's cardiac phenotype typically determines urgency, while the syndrome determines surveillance duration and depth. A ductal-dependent arch requires prostaglandin E1 and cardiac-center care regardless of syndrome, while Turner syndrome changes lifelong aortic and blood pressure monitoring. Complete atrioventricular septal defect requires repair planning regardless of karyotype, while Down syndrome changes pulmonary hypertension assessment and feeding strategies. Supravalvar aortic stenosis requires coronary assessment, while Williams syndrome changes anesthesia risk. Earlier cardiology reassessment is warranted for cyanosis, failed pulse oximetry screening, respiratory distress, shock,

weak pulses, poor feeding, poor growth, worsening outflow gradient, worsening valve regurgitation, rising estimated right ventricular pressure, pulmonary hypertension concern, ventricular dysfunction, myocardial fibrosis, arrhythmia, hypertension, syncope, chest pain, aortic growth, obstructive cardiac tumor or planned sedation, catheterization, surgery, transition, or pregnancy counseling. Common escalation triggers and actions are summarized in Table 2.

CONCLUSION

Syndromic pediatric cardiology is most valuable when the syndrome label is transformed into a timely management pathway. Down syndrome requires universal echocardiography and early assessment for shunt physiology and pulmonary hypertension; 22q11.2 deletion syndrome requires cardiac evaluation that accounts for conotruncal lesions, arch anomalies, hypocalcemia, immune defects, airway anomalies, and feeding difficulty; Turner syndrome requires lifelong aortic imaging and blood pressure monitoring; Noonan syndrome and other RASopathies require outflow, myocardial, rhythm, and bleeding-risk assessment; Williams syndrome requires arteriopathy, coronary, hypertension, and anesthesia-risk assessment; heritable aortopathies require aortic and systemic vascular imaging; and Duchenne muscular dystrophy requires cardiomyopathy assessment from diagnosis. The practical sequence is to define the lesion, apply physiology and disposition, modify for the syndrome, set the next reevaluation time point, and record one finding expected to change management.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Kebede AF. Cardiac care of children with common genetic syndromes: a practical review for pediatricians and pediatric cardiologists. *Int J Contemp Pediatr* 2026;13:1260-8.