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CCS Consensus Conference 2001 update: Recommendations for the Management of Adults with Congenital Heart Disease Part I

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The authors of this second Consensus Conference Report on Adult Congenital Heart Disease (ACHD) are grateful to the Canadian Cardiovascular Society (CCS) and its Council for the opportunity to update and assemble the document, which follows.

Important advances have been made in the field of adult congenital cardiology since the 1996 Consensus Conference Report was published (1), which led to the decision to update the recommendations. As well, over 160 new references have been added. Sections on marfan syndrome, single ventricle and cyanotic patients have been added. Prevalence, genetics, pregnancy and arrhythmias for each specific cardiac lesion have been incorporated. The recommendations that follow are the best available given the present knowledge.

These recommendations have been written for cardiologists, cardiac surgeons and other health care professionals who are not experts in this field. This is important to state, because an audience more or less knowledgeable about the subject would require a different amount of background information and depth of treatment of the material.

The panelists are convinced that the interests of any but the most simple patients are best served by involving what are called 'national or regional ACHD centres'. The knowledge and experience in the care of these patients should be focused, so that competence and skills become available as quickly as possible. This recommendation is not intended to stand in the way of involving local physicians in the care of these patients as collaborating members of a team with the best interests of the patients at heart. Almost all of these patients require primary care. Many would benefit from periodic contact with a cardiologist in their community, along with their specialist at the national or regional ACHD centre.

This Consensus Conference on the Management of Adults with Congenital Heart Disease is an update of the previous document published in The Canadian Journal of Cardiology *1998;14:395-452. The entire consensus statement will be published in three consecutive issues of* The Canadian Journal of Cardiology

The Congenital Heart Disease Committee of the American College of Cardiology, the Council on Cardiovascular Disease in the Young of the American Heart Association, the Grown-Up Congenital Heart Working Group of the European Society of Cardiology, the International Society for Adult Congenital Cardiac Disease and the Japanese Society for Adult Congenital Heart Disease have all endorsed this document

One of the problems and challenges of ACHD is the large number of different lesions and situations that may be encountered. Those specializing in the area have worked hard to attain the competence and confidence that they have, yet regularly continue to be unclear about managing individual patients. We have great respect for the seemingly endless scenarios that we encounter.

Patients with congenital heart disease (CHD) are interesting to have in one's practice, but they should be accepted either collaboratively with a national or regional ACHD centre, or after one has concluded that the patient does not need a referral to such a centre. The natural interest in 'collecting a few congenitals' should be resisted until this test has been run. This principle applies as much in a surgical as in a medical practice.

Canada is fortunate to have a nationwide group of national and regional ACHD centres called the Canadian Adult Congenital Heart (CACH) Network (Appendix 1). We encourage Canadian readers to make use of these facilities, and the skills and experience they represent. More information can be obtained on the Internet at www.cachnet.org.

Another aspect of this consensus conference update is that it will remain available on the Internet at www.cachnet.org, at www.achd-library.com and at www.ccs.ca.

In keeping with the origins of the panelists, this document has been endorsed by the most important societies with an interest in this field. We have written this material in as user-friendly a fashion as possible. We envisaged a clinician looking up a lesion, and wishing to see the recommendations at a glance, rather than having to refer to other sections of the report. This has led to some repetition for the reader who begins at the beginning and ends at the end. *The repetitive portions are printed in italics to reduce frustrations resulting from this style*. We also committed to not writing a textbook, even though a good and current one is needed for an audience such as ours. We have focused on the principles of management of these patients, leaving latitude where possible for the clinician to exercise judgement. We wish to guide, but not to constrain unduly. We have given weight to our management recommendations. The scales that we used are shown in Appendix II. We have used standards similar to those used in past CCS Consensus Conferences.

We hope that these recommendations will be helpful to the patients in whose interests we have written them, and to those who care for them. Canadians have made important contributions to the management of patients with CHD. We join with our international colleagues in hoping that this report will follow in this tradition.

CHOICE OF PANELISTS

The CCS invited Dr Gary Webb (president of the CACH Network) and Dr Judith Therrien to lead the process, and endorsed the membership of the primary and secondary panels. As is apparent from the panel memberships, the Grown-Up Congenital Heart Working Group of the European Society of Cardiology and the International Society for Adult Congenital Cardiac Disease contributed many members to this process. While published in Canada, this is truly an international document. Further, the panels were selected to receive input from various interested groups (adult/pediatric cardiology, cardiac surgery, obstetrics, genetics, nurse practitioner), and from the various regions of Canada, the United States, Europe and Japan.

Most of the panelists worked very hard reviewing many drafts and offering suggestions for improvement. The panel had almost no difficulty in reaching agreement on the statements made. Debate occurred only where there were insufficient data to decide a point.

A glossary defining the many unusual terms used in this field has been prepared as a companion document; space does not permit publishing this in this journal. We refer you to www.ccs.org and www.achd-library.com.

GENERAL RECOMMENDATIONS

Part I – Levels of care for adult patients with CHD

Care of adult patients with CHD should be available at several different levels. A national ACHD centre is one that can provide all needed services to ACHD patients. The CACH Network has recommended the maintenance or establishment of five 'national' centres in Canada (population 31 million), one in each of the five regions of the country. A regional ACHD centre is one that has the essential resources required for an ACHD centre (two ACHD cardiologists and excellent echocardiography facilities), plus any other resources that they may have beyond these. Such centres would provide most patient care, but would refer to a national centre when their resources are required (eg, congenital heart surgery, special electrophysiology services).

A national 'full service' ACHD centre:

- Should have all (or almost all) of the components described below in the ideal national centre
- May provide care to any patient with congenital or heritable cardiovascular disease
- Would usually serve a population base of three to 10 million

A regional ACHD centre:

- Will have a minimum of two cardiologists (either adult or pediatric) with special skills, training or experience in the care of adult patients with CHD, and highly skilled echocardiographic services; beyond this, other components of the national ACHD centre described below may be available, depending on local resources and needs
- May provide care to any patient with congenital or heritable cardiovascular disease within the constraints of available resources
- Would usually serve a population base of up to two million

An individual specialist/cardiologist:

- Provides specialist care to patients with the types of disorders listed in Appendix III, without there being a need to involve an ACHD centre; when such patients require special interventions (eg, cardiac surgery, electrophysiology study), referral to a national or regional ACHD centre is still recommended, unless these matters have nothing to do with the CHD
- Participates in the care of patients with the types of disorders listed in Appendix III in collaboration with the staff of a regional or national ACHD centre

An individual primary caregiver:

- May reasonably provide cardiovascular follow-up for some of these patients (see categories with asterisks in Appendix IV) without specialist referral unless circumstances warrant
- Should only manage other patients with congenital and heritable cardiovascular disease in collaboration with the staff in a regional or national ACHD centre

Part II – Description of an ideal national ACHD centre

The purpose of the ACHD centre is as follows.

- To optimize care for all adult patients with CHD and to reduce errors in care occurring in such patients
- To consolidate specialized resources required for the care of adult congenital cardiac patients
- To provide sufficient patient numbers to facilitate the training of personnel wishing to develop expertise in ACHD, and to maintain staff and faculty competence and special skills in the treatment of patients with ACHD
- To facilitate research in this unique population to approach the ideal of evidence-based care, and to promote a more complete understanding of the processes affecting these patients
- To offer educational opportunities to primary caregivers, cardiologists and surgeons so that they may contribute optimally to patient management
- To provide a readily available source of information and expert opinion for patients and doctors
- To help organize support groups for patients
- To provide information for government and act as the representative of the specialty

Human resources

Human resources should include the following personnel, who have additional experience or training in the management of adults with CHD, as well as adult cardiology in general, and knowledge of the terminology and issues of concern in pediatric CHD patients.

- Two or more cardiologists trained in adult cardiology and/or pediatric cardiology and with special training or experience in the care of ACHD patient
- At least two surgeons with experience in all aspects of CHD surgery (usually based in a pediatric unit)
- Two or more electrophysiologists with training or experience in congenital cardiac electrophysiology and with relevant pacemaker expertise
- Two or more interventional cardiologists with training or experience in noncoronary interventional procedures
- Two or more medical imaging specialists (eg, magnetic resonance imaging [MRI], computed tomography [CT], nuclear cardiology)
- Two or more cardiac anesthetists with special ACHD knowledge and skills
- A well functioning intensive care team
- A well functioning transplant team or a formal association with a transplant centre
- A social work and vocational counselling service
- Specialized nursing staff (eg, nurse clinicians or specialists) with experience in dealing with CHD and adult cardiology
- A cardiac pathologist with substantial experience in congenital heart malformations
- Consultants in the fields of obstetrics and gynecology, genetics, nephrology, pulmonary medicine, hematology, neurology, rheumatology, cardiac rehabilitation, infectious diseases and psychiatry/psychology

Technical infrastructure

The following resources should be available.

- Echocardiography (including transesophageal, intra-operative and fetal echocardiography)
- A cardiac catheterization laboratory with biplane angiography for both diagnostic and interventional procedures
- An electrophysiology laboratory capable of sophisticated mapping and radiofrequency ablation
- An operating room and team capable of providing both pump and nonpump facilities, both electively and as emergencies
- Other appropriate inpatient facilities (intensive care unit [ICU]), step-down and inpatient unit)
- Diagnostic imaging with full capabilities (including cardiovascular radiology, CT, MRI, nuclear cardiology)

- Pacemaker clinic with expertise in advanced pacing and defibrillation technology
- Holter monitoring
- Cardiopulmonary function testing, exercise testing and oxygen saturation capability
- Cardiac pathology
- Data collection system

The functions of the ACHD centre are as follows.

- To provide optimal care to adults with CHD
- To work with colleagues at the usually adjacent pediatric centres to optimize the transition and transfer of patient care from a pediatric to an adult facility
- To hold regular conferences in which management of patients is discussed and decisions are made through consensus
- To ensure appropriate and timely communication with referring physicians and their staff
- To ensure appropriate links between the national ACHD centre and support services within the academic medical centre
- To implement and ensure processes for evaluating feedback and continuous quality improvement in patient care and teaching within the national ACHD centre
- To ensure cooperation and collaboration with other ACHD centres
- To participate in clinical trials with other centres both nationally and internationally, and to help develop new knowledge through, when appropriate, the sharing of linked databases established in accordance with legal and ethical requirements
- To establish and evaluate ongoing training programs for both cardiologists and surgeons interested in developing expertise in the treatment of patients with ACHD, and for all associated staff, including technologists, nurses, psychologists, physiotherapists, occupational therapists and others
- To maintain a database on all patients managed through that centre

Part III – Indications for referral to a national or regional ACHD centre

An adult or older adolescent patient would be referred to an ACHD centre for the following.

- Assessment of suspected or known CHD
- Follow up and continuing care of patients with lesions (Appendix III)
- Some types of surgical or nonsurgical intervention
- Assessment regarding noncardiac surgery or pregnancy

Part IV – Specialists involved in the management of ACHD patients

The following specialists should be involved in the management of patients with ACHD.

- Cardiac surgeons operating on adults and adolescents with CHD should have completed training in cardiothoracic or cardiac surgery to prevailing national standards, undergone formal training in surgery for congenital heart malformations and obtained extensive experience in the surgical management of adult patients with CHD.
- Cardiac anesthetists involved in surgery on adults with CHD must have had specialized training and/or extensive experience in the treatment of patients with CHD, adult patients undergoing other types of cardiac surgery and the anesthetic management of problems such as cyanosis, elevated pulmonary vascular resistance or severe outflow obstruction.
- Adult ACHD cardiologists (especially those still to be trained) should have completed full adult cardiology training, and have taken at least one year of supplemental training in CHD as it applies to adolescents and adults. Guidelines have been published. Their ability to serve the interests of these patients will be in proportion to the amount of time that they have spent in training, continuing education and clinical experience in the management of these patients.
- Pediatric ACHD cardiologists (especially those still to be trained) should have completed pediatric cardiology training and have taken at least one year of supplemental training in adult cardiology and ACHD so as to be able to recognize and deal with noncongenital issues that will arise in these patients. Their ability to serve the interests of these patients will be in proportion to the amount of time that they have spent in training, continuing education and clinical experience in the management of these patients.
- Echocardiographers responsible for recording and interpreting echocardiograms in adults with CHD should be appropriately trained (level 3 echocardiography training) and have a thorough understanding of the technical principles of echocardiography and a thorough knowledge of the anatomy, hemodynamics and pathology of both acquired and CHD to obtain, correlate and record efficiently the echocardiographic findings. The Canadian Society of Echocardiography on Physician Training recommends one year of echocardiography fellowship to attain level 3 training (2). Training in transesophageal echocardiography is also vital.

Part V – Specific issues in the care of patients with ACHD

Noncardiac surgery

Performance of any surgical procedures in most adult patients with CHD carries a greater risk than in the general population. Evaluation in an ACHD centre before surgery is recommended, and in the case of unoperated or complex ACHD, it is recommended (where feasible) that the surgery be carried out in the ACHD centre by experienced cardiac anesthetists. This is strongly recommended for cyanotic patients, patients with pulmonary hypertension or patients with some rhythm abnormalities. Pregnant women with CHD should be managed by the patient's obstetrician and ACHD cardiologist together with a cardiac anesthetist, if necessary. In most cases, an obstetrician knowledgeable in the management of ACHD is optimal. Postoperatively, the patients with CHD may need ICU or monitoring facilities even for relatively minor procedures.

Dental care

Regular dental care, often in a hospital setting, is needed by most adult patients with CHD to decrease the likelihood of caries, abscesses or periodontal disease, all of which contribute to the increased incidence of infective endocarditis. There is justification for government subsidization of dental care in patients unable to afford it. Endocarditis prophylaxis, both antibiotics and daily teeth and gum care, are recommended.

Informed consent

Despite its lifelong presence, most adolescents and young adults with CHD have inadequate knowledge about their cardiac conditions. Health care providers must assess each patient's knowledge of his or her condition and give appropriate information to enable independent decision-making about choices in care. Adults with CHD should be encouraged to understand not only their disease, but also the medications that they use. They should be involved in major management decisions or decisions involving invasive procedures. Patients should be encouraged to inform their specialists of any new events that may occur. Further involvement of patients in the evaluation of processes and programs, and in the planning of research trials within the constraints of their motivation and capacity to understand them, is ideal.

Advance directives and palliative care

Patients should be made aware of the availability of advance directives that are legally binding. Their use may reduce uncertainty when caring for critically ill individuals. Likewise, the role of nonintervention or of palliative care as a treatment modality should be presented in a realistic, unbiased and acceptable manner as one of the options to patients making decisions about interventions or procedures. The probable result of this clinical pathway should be objectively explained with comparison of outcomes with other interventions when this information is known.

Autodonation of blood

Patients should be made aware of the possibility of autologous donation or directed donation (from family members) of blood before cardiac surgery if such facilities exist.

SECTION I – ATRIAL SEPTAL DEFECT

Part I – Background information

Atrial septal defect (ASD) includes ostium secundum, sinus venosus and coronary sinus. Ostium primum (partial atrioventricular septal defect [AVSD]) is discussed in Section III.

A 'clinically significant' ASD:

- Causes right heart volume and sometimes pressure overload
- May cause exercise limitation
- May be associated with atrial arrhythmias (atrial fibrillation, atrial flutter, usually over age 30 years)
- May cause late right heart failure (usually over age 40 years)
- May permit paradoxical embolism resulting in transient ischemic attack or stroke
- May lead to pulmonary hypertension, although pulmonary hypertension may also develop from other causes

Part II – Prevalence and genetics

Although usually sporadic, some ASDs are inherited as an autosomal dominant gene and/or are associated with other congenital lesions (eg, Holt-Oram syndrome).

Part III – History and management of unoperated patients

Most patients with 'significant' ASDs (see above) eventually develop symptoms, although the timing of symptom development is unpredictable and may be after the fifth decade. The most common symptoms are exercise intolerance (dyspnea and fatigue) and symptomatic supraventricular arrhythmias (atrial fibrillation, atrial flutter or sick sinus syndrome). Any condition causing reduced left ventricular compliance (eg, left ventricular hypertrophy due to hypertension, cardiomyopathy or myocardial infarction) tends to increase the left-to-right shunt through an ASD and worsen symptoms. Their prevention and/or early treatment should be addressed.

In Lutembacher syndrome (congenital ASD with acquired mitral stenosis), the mitral valve obstruction increases the left-to-right shunt. The combination of lesions is usually poorly tolerated.

Part IV – Diagnostic recommendations

An adequate diagnostic workup:

- Documents the presence and type of ASD(s)
- Determines the size (diameter) of the defect(s)

- Determines the functional importance of the defect by
  - shunt size (pulmonary to systemic flow ratio [Qp/Qs]);
  - right ventricular size, function and volume overload and right atrial size; or
  - pulmonary artery pressures and, if elevated, pulmonary vascular resistance
- Identifies other associated conditions that may influence management (eg, anomalous pulmonary venous connection, significant valve disease or coronary artery disease)

The initial workup should include at a minimum:

- *A thorough clinical assessment*
- *Electrocardiogram*
- *Chest x-ray*
- *Transthoracic echocardiography (TTE)/Doppler evaluation by an appropriately trained individual*
- Transesophageal echocardiography (TEE)/Doppler examination to prove the existence of an ASD, better define its (their) location(s) and size(s) and shape(s), assess pulmonary venous connections, and evaluate the cardiac valves, if this information is not provided by TTE; a transesophageal examination is essential to determine whether the ASD is suitable for device closure and must be performed before the procedure
- Resting oxygen saturation

The diagnostic workup may require:

- Heart catheterization (if determination of pulmonary artery pressures and resistances is of concern, to assess pulmonary vascular reactivity or to delineate anomalous pulmonary venous connections)
- *Coronary angiography in patients at high risk of coronary artery disease or in patients over the age of 40 years if surgical repair is planned*
- MRI to prove the existence of an ASD or to assess pulmonary venous connections if doubts remain after other imaging modalities. MRI can also be used to estimate Qp/Qs
- Oxygen saturation with exercise if there is any suggestion of pulmonary hypertension. If there is severe pulmonary hypertension or resting desaturation of less than 85%, the patient should not be exercised
- *Open lung biopsy should only be considered when the reversibility of the pulmonary hypertension is uncertain from the hemodynamic data; it is potentially hazardous and should be done only at centres with substantial relevant experience in CHD*

Part V – Indications for intervention

Indications for closure are debated. There is little proof of firm guidelines. We offer a consensus view.

The mere presence of a 'significant' ASD may warrant intervention especially if there is a significant shunt (greater than two to one).
If pulmonary hypertension is present (pulmonary artery pressure [PAP] greater than two-thirds systemic arterial blood pressure [SABP], or pulmonary arteriolar resistance greater than two-thirds systemic arteriolar resistance), there must be a net left-to-right shunt of at least 1.5 to one, or evidence of pulmonary artery reactivity when challenged with a pulmonary vasodilator (eg, oxygen, nitric oxide and/or prostaglandins) or lung biopsy evidence that pulmonary arterial changes are potentially reversible (Heath Edwards grade II to III or less).
A cryptogenic cerebrovascular event in the presence of a small ASD or patent foramen ovale, and right-to-left shunting demonstrated on contrast echocardiogram may warrant ASD closure. This indication, however, is 'softer' than the others.
Grade: C
Level: III
References: 3-8

If closure of the atrial septal defects is planned, it is recommended that it be performed without undue delay (before age 25 years for mortality benefit, and probably before age 40 years for arrhythmia benefit). As a rule, younger patients have a better outlook after repair (3,9,10).

Transvenous pacing should be avoided in patients with unrepaired ASDs because paradoxical emboli may occur. For the same reason, venous thromboemboli from any source are a potential hazard.
Grade: C
Level: V
References: 11,12

Part VI – Surgical/interventional technical options

Device closure may be offered as an alternative to surgical closure to patients with secundum ASD of up to 36 to 38 mm in diameter. The intervention should be performed under general anesthesia with transesophageal guidance in centres and by individuals with a commitment to the technique and to its clinical evaluation.
Grade: C
Level: V
References: 13-17

Surgical closure may also be offered and may be especially attractive should the patient prefer the time-honoured surgical approach, or especially if atrial arrhythmia surgery (atrial maze procedure for atrial fibrillation and radiofrequency or cryoablation for atrial flutter) may be offered concurrently.

The availability of an inframammary or right minithoracotomy or ministernotomy approach to a typical secundum ASD should be made known to potentially interested patients considering surgery.

Patients with a sinus venosus ASD or ostium primum ASD cannot be closed by percutaneous devices and should be surgically repaired by congenital heart surgeons.
Grade: C
Level: V
References: 18,19

Part VII – Surgical/interventional outcomes

Device closure

Early and intermediate follow-up are excellent after device closure. The intermediate results are comparable with those of surgery, with a high rate of shunt closure and few major complications. The long term outcome is unknown. Longer follow-up is needed to determine the incidence of arrhythmias and thromboembolic complications late after device closure.

Functional capacity improves, and supraventricular arrhythmias are better tolerated and more responsive to pharmacological management.

Surgical closure

For secundum ASD without pulmonary hypertension, surgical closure should result in a very low (less than 1%) operative mortality. Early and long term follow-up are excellent.

Following surgical repair, preoperative symptoms, if any, should decrease or abate. Pre-existing atrial flutter and fibrillation may persist unless cryo- or radiofrequency ablation (for the former) or a right atrial maze including pulmonary vein encirclement (for the latter) has been performed. Likewise, atrial flutter and/or fibrillation may arise de novo after repair, but are better tolerated and often more responsive to antiarrhythmic therapy.

Left ventricular failure may occur in patients with associated cardiovascular disease (eg, coronary artery disease, hypertension, mitral valve incompetence).

Postoperative ASD patients are especially prone to cardiac tamponade for the first several weeks after surgery.
Grade: Consensus

Part VIII – Arrhythmias

Late atrial fibrillation may occur in up to one-third of patients, especially in adults older than 40 years and/or if atrial arrhythmias were present preoperatively. Physicians may elect to provide anticoagulation therapy with warfarin to these high risk patients for the first six months after operation because of the risk of atrial fibrillation and stroke. Anticoagulation treatment can probably be discontinued thereafter if the patient remains arrhythmia-free and there are no other risk factors.

The presence of preoperative atrial flutter or fibrillation may warrant surgical closure of the defect with concomitant cryosurgical or ablative therapy, or an atrial maze procedure.
Grade: C
Level: V
Reference: 20

If atrial fibrillation occurs, both anticoagulants and antiarrhythmic therapy are usually indicated.
Grade: A
Level: I
Reference: 21

Part IX – Pregnancy

Pregnancy is well tolerated in patients after ASD closure. Pregnancy is also well tolerated in women with unrepaired ASDs, but the risk of paradoxical embolism is increased during pregnancy as well as during the postpartum period.

Pregnancy is contraindicated in patients with Eisenmenger syndrome because of the high maternal (up to 50%) and fetal (up to 60%) mortality.
Grade: C
Level: V
Reference: 22

Part X – Follow-up

ASD patients with the following characteristics require periodic follow up by an ACHD cardiologist.

- Repaired as adults
- Elevated pulmonary artery pressures at the time of repair
- Atrial arrhythmias pre- or postoperatively
- Ventricular dysfunction preoperatively
- Coexisting heart disease (eg, coronary artery disease, valvular heart disease, hypertension)
- Those with device closure need follow-up in specialized centres with serial electrocardiograms and echocardiograms to determine the late outcomes of these new techniques

Endocarditis prophylaxis and acetylsalicylic acid are recommended for six months following device closure.
Grade: Consensus

SECTION II – VENTRICULAR SEPTAL DEFECT

Part I – Background information

Only isolated ventricular septal defects (VSDs) are considered.

Hemodynamic severity grading of isolated VSDs in adults:

- Small: Pulmonary to aortic systolic pressure ratio less than 0.3, and Qp/Qs less than 1.4
- Moderate: Systolic pressure ratio greater than 0.3 and Qp/Qs 1.4 to 2.2
- Large: Systolic pressure ratio greater than 0.3 and Qp/Qs greater than 2.2
- Eisenmenger: Systolic pressure ratio greater than 0.9 and Qp/Qs less than 1.5

Physiological classification of isolated VSD in adults:

- Restrictive: Right ventricular pressure less than left ventricular pressure in the absence of right ventricular outflow tract obstruction.
- Nonrestrictive: Equal right and left ventricular pressures in the absence of right ventricular outflow tract obstruction.

Clinical severity grading of isolated VSDs in adults:

- Small: Causes negligible hemodynamic changes. Left ventrular size is usually normal without any pulmonary hypertension.
- Moderate: Causes enlargement of left ventricle and left atrium, and usually some pulmonary hypertension (reversible).
- Large: Results in pulmonary vascular obstructive disease and Eisenmenger physiology unless there is coexistent right ventricular outflow tract obstruction.

Pathological/surgical classification:

- Perimembranous: Bordered by fibrous continuity of an atrioventricular valve and an arterial valve, usually with inlet or outlet extension.
- Muscular: Bordered by muscle rim, usually trabecular.
- Doubly committed: Bordered by fibrous continuity of both the aortic and the pulmonary valve.

VSDs may coexist with other cardiac lesions (especially valvar or subvalvar pulmonary stenosis) or result in secondary infundibular hypertrophy, right ventricular outflow obstruction and aortic regurgitation from aortic cusp prolapse.

Part II – Prevalence and genetics

Doubly committed VSDs are more common in Asian patients.

Part III – History and management of unoperated patients

Small VSDs are associated with a relatively high risk of endocarditis, but otherwise patients enjoy a normal life expectancy. Atrial arrhythmias may occur. Spontaneous closure of VSDs can still occur occasionally in adult life.

Moderate VSDs are unusual in the adult but may occur when a prolapsing aortic valve cusp partially obstructs the defect. They are associated with the development of left heart dilation and shunt-related pulmonary hypertension (which often reverses with correction of the defect), and resultant congestive heart failure and atrial fibrillation, as well as the risk of endocarditis.

Large VSDs without pulmonary hypertension exist in adults only when associated with obstruction to right ventricular outflow and are rare. Some are cyanotic because of more severe right ventricular outflow tract obstruction at the infundibular or valvular level.

VSD patients with Eisenmenger syndrome (see section XV) are at continuous risk of mortality and morbidity. *Poor prognostic features are thought to be atrial flutter/fibrillation, syncope, heart failure, hemoptysis and aneurysmal dilation of proximal hypertensive pulmonary arteries, which may rupture. Laminated thrombus in the dilated pulmonary arteries can be found.*

Five per cent of VSDs develop aortic valve regurgitation. Patients with doubly committed subarterial VSDs are more

likely to develop aortic regurgitation from progressive prolapse of the aortic valve cusps than those with a perimembranous VSD (23).

Part IV – Diagnostic recommendations

An adequate diagnostic workup

- Documents the number and type(s) of VSD.
- Determines the size (restrictive or nonrestrictive) and functional importance (left-to-right shunt estimate, left and right ventricular size/function, ventricular volume and pressure overload, pulmonary artery pressure and resistance) of the defect
- Identifies other associated conditions that may influence management (aortic regurgitation, subaortic stenosis, right ventricular outflow obstruction, significant valve disease, coronary artery disease, coarctation of the aorta)

The initial workup should include at a minimum

- *A thorough clinical assessment*
- *Electrocardiogram*
- *Chest x-ray*
- *TTE/Doppler evaluation by an appropriately trained individual*

The diagnostic workup may require

- Oximetry
- Heart catheterization to determine pulmonary artery pressures and resistances (with or without reversibility using oxygen, nitric oxide and/or prostaglandins); to assess intracardiac shunting; to evaluate associated lesions, particularly if aortic regurgitation is present; and to exclude multiple VSDs
- *Coronary angiography in patients at risk of coronary artery disease or in patients over the age of 40 years if a surgical repair is planned*
- *Open lung biopsy should only be considered when the reversibility of the pulmonary hypertension is uncertain from the hemodynamic data. It is potentially hazardous and should be done only at centres with substantial relevant experience in CHD*
- *MRI occasionally to confirm the presence or absence of other associated lesions or to help define the anatomy of the aortic cusps to eliminate aortic valve prolapse*. MRI can also be used to estimate Qp/Qs

Part V – Indications for intervention

The following situations warrant operative closure.

- The presence of a 'significant' VSD (symptomatic Qp/Qs=2/1, pulmonary artery systolic pressure greater than 50 mmHg), deteriorating ventricular function due to volume (left ventricle) or pressure (right ventricle) overload.
- Significant right ventricular outflow tract obstruction (peak to peak catheterization gradient of 50 mmHg, or peak instantaneous gradient greater than 70 mmHg)
- A perimembranous or doubly committed VSD with more than mild aortic incompetence
- *In the presence of severe pulmonary hypertension (PAP greater than two-thirds SABP, or pulmonary arteriolar resistance greater than two-thirds systemic arteriolar resistance), there must be a net left-to-right shunt of at least 1.5 to one or evidence of pulmonary artery reactivity when challenged with a pulmonary vasodilator (eg, oxygen, nitric oxide and/or prostaglandins) or lung biopsy evidence that pulmonary arterial changes are potentially reversible (Heath Edwards grade II-III or less).*

Grade: C
Level: IV
References: 24-29

Endocarditis (especially recurrent) may be an indication for operative closure (30).

Transvenous pacing should be avoided where possible in all patients with VSDs because paradoxical emboli may occur. For the same reason, venous thromboemboli from any source are a potential hazard.
Grade: C
Level: V
Reference: 11

Part VI – Surgical/interventional technical options

Patients with an isolated VSD with or without associated lesions (right ventricular outflow tract obstruction, aortic valve prolapse, subaortic stenosis or infective endocarditis) should be repaired by congenital heart surgeons.
Grade: C
Level: V
References: 18,19

Device closure of VSDs may be performed in the setting of isolated trabecular muscular VSDs but are still considered an experimental procedure for perimembranous VSDs (31,32).

Part VII – Surgical/interventional outcomes

Successful closure is associated with excellent survival if ventricular function is normal. Elevated pulmonary artery pressures preoperatively may progress, regress or remain unchanged postoperatively.

Part VIII – Arrhythmias

Atrial fibrillation may occur, especially if there has been longstanding volume overload of the left heart, or if other reasons for left atrial dilation are present. Late ventricular arrhythmias and sudden death are potential risks, especially in patients repaired late in life (33,34). Complete heart block may also occur after surgical repair.

Part IX – Pregnancy

Pregnancy is well tolerated in women with small or moderate VSD and in women with repaired VSDs.

Pregnancy is contraindicated in Eisenmenger syndrome because of high maternal (up to 50%) and fetal (up to 60%) mortality.
Grade: C
Level: V
Reference: 22

Part X – Follow-up

Patients with the following problems benefit from periodic evaluation by an ACHD cardiologist.

- Patch leaks or residual VSDs (which seldom require reoperation)
- Elevated pulmonary vascular resistance at the time of surgery
- Aortic valve surgery
- Late repair of moderate or large defects
- Significant atrial or ventricular arrhythmias
- Associated cardiac lesions (eg, right ventricular outflow tract obstruction or aortic regurgitation)

Endocarditis prophylaxis is recommended for six months following VSD closure or for life if any residual defect persists.
Grade: Consensus

SECTION III – AVSD

Part I – Background information

Definition: The terms 'atrioventricular (septal) defects', 'atrioventricular canal defects' and 'endocardial cushion defects' can be used interchangeably to describe this group of defects. AVSD cover a spectrum of anomalies caused by abnormal development of the endocardial cushions. The defect may be only at the atrial level (ostium primum ASD) or may include an inlet-type ventricular septal defect (intermediate AVSD when the VSD is restrictive or complete form of AVSD when the VSD is nonrestrictive). The atrioventricular valves are fundamentally abnormal, being derived from five leaflets (a right anterosuperior leaflet, a right inferior leaflet, a superior bridging leaflet, an inferior bridging leaflet and a left mural leaflet). This may result in separate right and left atrioventricular valves (with the left atrioventricular valve having a 'cleft' at the junction of the superior and inferior bridging leaflets) or a common valve (Table 1).

TABLE 1
Classification of atrioventricular (AV) septal defects (AVSDs)

AVSD	Characteristic
Partial	The ventricular septum is intact There is almost always a primum ASD 'cleft' in the left AV (mitral) valve There are two separate AV valve annuli
Intermediate	The rarest form and a part of a spectrum between complete and partial AVSD Characterized by a restrictive VSD, a primum ASD and a cleft mitral valve The anterior and posterior bridging leaflets are fused, giving two distinct AV valve components
Complete	A nonrestrictive inlet-type VSD Usually a primum ASD (rarely, the atrial septum may be intact) There is a common AV orifice

Part II – Prevalence and genetics

AVSD may coexist with other lesions, both cardiac and noncardiac. Down syndrome occurs in 35% of patients with AVSD. Most complete AVSDs occur in Down syndrome patients (greater than 75%). Patients with Down syndrome have a premature tendency for pulmonary vascular disease, irrespective of the type of AVSD. Most partial AVSDs occur in non-Down syndrome patients (greater than 90%). AVSD may occur in association with tetralogy of Fallot and other forms of complex CHD.

Part III – History and management of unoperated patients

Clinical presentation of unoperated patients depends on the presence and size of the ASD and VSD, and competence of the left atrioventricular ('mitral') valve.

Clinical presentation may take several forms:

- Symptoms of heart failure or pulmonary vascular disease
- Atrial arrhythmias, nodal rhythm or complete heart block
- Subaortic stenosis may or may not be present initially but may develop or progress
- No symptoms

Partial or intermediate AVSD

Presentation of an unrepaired partial (ostium primum ASD) or intermediate AVSD as an adult is not uncommon. Symptoms include decreased exercise tolerance, fatigue, dyspnea, arrhythmias and recurrent chest infections. Symptoms increase with age, and most adults are symptomatic by 40 years of age.

Complete AVSD

Most patients with complete defects have been repaired in infancy, although some may have been palliated in the past with pulmonary artery bands and have variable degrees of pulmonary vascular obstructive disease. The history of unoperated complete AVSD is that of Eisenmenger syndrome (Section XV). AVSD with Eisenmenger syndrome seems to have a worse prognosis than ASD, VSD or PDA with Eisenmenger. *Poor prognostic features are thought to be atrial flutter/fibrillation, syncope, heart failure and hemoptysis.*

Part IV – Diagnostic recommendations

An adequate diagnostic workup:

- Documents the presence of each component of the AVSD and whether the ventricular chamber sizes are 'balanced' (although this is usually a pediatric issue)
- Assesses the magnitude and direction of intracardiac shunting
- Documents the pulmonary artery pressure
- Documents abnormalities of the atrioventricular valves and their connections (straddling of the atrioventricular valves or overriding of the atrioventricular annulus) and assesses the severity of atrioventricular valve regurgitation, if any
- Documents the presence or absence of subaortic stenosis, which may occasionally require provocative testing with isoproterenol, although it may be impossible to document a gradient in the presence of a nonrestrictive VSD
- Identifies the presence of associated abnormalities (cardiac and noncardiac), which may affect management (eg, pulmonary hypertension, tetralogy of Fallot, patent ductus arteriosis [PDA], muscular VSDs, aortic coarctation or Down syndrome)

The initial workup should include at minimum:

- *A thorough clinical assessment* paying particular attention to atrioventricular valve regurgitation
- *Electrocardiogram*
- *Chest x-ray*
- *TTE/Doppler evaluation by an appropriately trained individual*

The diagnostic work-up may require:

- TEE to determine the exact anatomy (if unclear after TTE), the presence of intracardiac shunts, chordal attachments, the presence and severity of left atrioventricular ('mitral') valve regurgitation (or stenosis if previous valve repair has been undertaken), the presence and severity of right atrioventricular valve regurgitation and subaortic stenosis
- Heart catheterization to determine the presence and magnitude of intracardiac shunts, pulmonary artery pressures and resistances, the severity of pulmonary vascular disease (with or without reversibility using oxygen, nitric oxide and/or prostaglandins), the presence and severity of left atrioventricular ('mitral') valve regurgitation (or stenosis, if previous valve repair has been undertaken), the presence and severity of subaortic stenosis (provocative testing may be necessary)
- *Coronary angiography in patients at risk of coronary artery disease or in patients over the age of 40 years if a surgical repair is planned*
- *Open lung biopsy should only be considered when the reversibility of the pulmonary hypertension is uncertain from the hemodynamic data. It is potentially hazardous and should be done only at centres with substantial relevant experience in CHD*
- Holter monitoring to assess atrioventricular block or other arrhythmia
- MRI to help define the anatomy. MRI can also be used to estimate Qp/Qs

Part V – Indications for intervention/reintervention

The following situations warrant intervention or reintervention.

- The unoperated AVSD with any sustained atrial arrhythmias, impaired ventricular function, right ventricular volume overload, attributable symptoms, heart failure, presumed paradoxic embolism or reversible pulmonary hypertension
- Persisting or new hemodynamically significant defects arising after the original repair
- Left atrioventricular ('mitral') valve regurgitation (or stenosis from previous repair) causing symptoms, atrial arrhythmia or deterioration in ventricular function.
- Significant subaortic obstruction (peak to peak catheterization gradient greater than 50 mmHg, or peak instantaneous gradient greater than 70 mmHg) may require intervention

Grade: C
Level: V
References: 35-37

Transvenous pacing should be avoided if there are residual interatrial or interventricular communications because paradoxical emboli may occur. For the same reason, venous thromboemboli from any source are a potential hazard.
Grade: C
Level: V
Reference: 11

Part VI – Surgical technical options

AVSD patients, including those with ostium primum ASD, left atrioventricular ('mitral') valve repair, subaortic stenosis or residual defects, should undergo operation by congenital heart surgeons.
Grade: C
Level: V
References: 18,19

When mitral valve repair is not possible, mitral valve replacement may be necessary. It should have a similar operative risk as routine mitral valve replacement, although the risk of complete atrioventricular block may be higher.

Part VII – Surgical outcomes

In the short term, the results of repair of partial AVSD are similar to those following closure of secundum ASD, but sequelae of left atrioventricular ('mitral') valve regurgitation, subaortic stenosis and atrioventricular block may develop or progress (38-42).

In general, late results after 'mitral' valvuloplasty for these patients have been excellent, with the need for surgical revision in about 5% to 10% of patients (39-41). Occasionally, repair of the abnormal left atrioventricular ('mitral') valve may result in a stenotic valve, which usually necessitates reoperation.

The likelihood of a residual left-to-right shunt from left atrium or left ventricle to right atrium is small. Subaortic stenosis develops or progresses in up to 5% of patients after repair, particularly in patients with primum ASD and some complete defects, especially if the left atrioventricular (mitral) valve has been replaced.

The long term results of repair of complete AVSD are not well known, but problems similar to those with partial AVSD are likely.

Part VIII – Arrhythmias

First degree atrioventricular block is common, and complete atrioventricular block may occur spontaneously or after repair. Sinus node dysfunction may also occur, especially after repair, and lead to brady- or tachyarrhythmias. Atrial flutter or fibrillation in the adult is not uncommon.

Part IX – Pregnancy

Pregnancy is well tolerated in patients with complete repair and no significant residual lesions.

Women in New York Heart Association class I and II with unoperated partial AVSD usually tolerate pregnancy very well, but have an increased risk of paradoxical embolization.
Consideration should be given to closure of any significant AVSD before pregnancy to minimize the risk of paradoxical emboli.
Grade: Consensus

Pregnancy is contraindicated in Eisenmenger syndrome because of the high maternal (up to 50%) and fetal (up to 60%) mortality.
Grade: C
Level: V
References: 22

Part X – Follow-up

All patients with AVSD require periodic follow up by an ACHD cardiologist because of the possibility of progressive atrioventricular valve regurgitation (or stenosis), the development of subaortic stenosis, the development of significant atrial arrhythmias or progression of the commonly present first degree atrioventricular block. Particular attention should be paid to those with pulmonary vascular disease present preoperatively. Endocarditis prophylaxis is recommended for six months following AVSD closure or for life if any residual defect persists.
Grade: Consensus

SECTION IV – PDA

Part I – Background information

The ductus arteriosus, in utero, connects the proximal left pulmonary artery to the descending aorta, just distal to the left subclavian artery. Failure of closure at birth represents a congenital malformation. A PDA in an adult is usually an isolated lesion.

Clinical severity grading of PDA in adults:

- Silent: Tiny PDA detected only by nonclinical means (usually echocardiography).
- Small: Audible continuous murmur. Causes negligible hemodynamic change. Normal left ventricular size without any pulmonary hypertension.
- Moderate: Audible continuous murmur. Wide pulse pressure (as in aortic regurgitation). Causes enlargement of the left ventricle and some pulmonary hypertension (usually reversible).
- Large: Usually does not exist in adults without Eisenmenger physiology.
- Eisenmenger: Continuous murmur is absent. Causes substantial pulmonary hypertension, differential hypoxemia and often differential cyanosis.

Part II – History and management of unoperated patients

The risk of endarteritis with small silent PDA is unknown but is likely very low (only sporadic case reports exist).

No intervention is indicated if a small silent PDA is detected.
Grade: Consensus

All other PDAs are associated with a risk of endarteritis (which may increase with increasing age). Patients with small PDAs have a normal life expectancy. A moderate PDA is unusual in the adult. It is associated with the development of left heart dilation and shunt-related pulmonary hypertension (which often reverses with correction of the defect). The majority of patients are symptomatic from dyspnea or palpitations (atrial arrhythmias), although frank heart failure is unusual. A large PDA is rare in the adult, most having been corrected in infancy and childhood.

Pulmonary hypertension is usual and may not reverse entirely with closure of the defect. Most patients are symptomatic from dyspnea or palpitations. Aneurysm formation of the duct is an uncommon but important complication.

Eisenmenger PDA has a prognosis similar to that of Eisenmenger VSD, although symptoms may be less marked and exercise tolerance better. Eisenmenger PDA is discussed further in section XV.

Part lII – Diagnostic recommendations

An initial diagnostic work-up:

- Documents the presence of PDA
- Determines the size (systemic-to-pulmonary shunt estimate) and functional importance (pulmonary artery pressures) of the defect. Shunt estimates are often inaccurate because of the difficulty in obtaining a representative pulmonary blood sample for saturation assessment
- Identifies whether a ductal aneurysm is present
- Identifies whether the duct is calcified if surgical repair is planned

The diagnostic work-up should include, at a minimum:

- *A thorough clinical assessment*
- *Electrocardiogram*
- *Chest x-ray*
- *TTE/Doppler evaluation by an appropriately trained individual*
- Oximetry (obtained on both fingers and toes)

The diagnostic work-up may require:

- Heart catheterization (to determine pulmonary artery pressures and resistances with testing of pulmonary vascular reactivity using prostacyclin, inhaled oxygen and nitric oxide if pulmonary arterial pressures are greater than two-thirds the systemic pressure)

- *Coronary angiography in patients at risk for coronary artery disease or in patients over 40 years if a surgical repair is planned*
- *Open lung biopsy should only be considered when the reversibility of the pulmonary hypertension is uncertain from the hemodynamic data. It is potentially hazardous and should be done only at centres with substantial relevant experience in CHD*
- MRI or CT scan to define the anatomy and detect ductal aneurysm or calcification. MRI can also be used to estimate Qp/Qs

Part IV – Indications for intervention

The following situations warrant intervention.

- The presence of a PDA (except the silent duct at one extreme and the presence of severe, irreversible pulmonary vascular disease at the other extreme)
- Closure of a small but audible PDA is usually recommended, although this indication remains controversial given the low perceived risk of endarteritis
- The occurrence of an episode of endarteritis on a clinically silent PDA
- *If pulmonary hypertension is present (PAP greater than two-thirds SABP or pulmonary arteriolar resistance exceeds two-thirds systemic arteriolar resistance), there must be a net left-to-right shunt of at least 1.5 to one, or evidence of pulmonary artery reactivity when challenged with a pulmonary vasodilator (eg, oxygen, nitric oxide, and/or prostaglandin$_1$) or lung biopsy evidence that pulmonary arterial changes are potentially reversible (Heath Edwards grade ll to III or less)*

Grade: C
Level: V
References: 25,43,44

Part V – Surgical/interventional technical options

Device closure is the preferred method for the small ductus and, when possible, should be planned at the same time as the diagnostic catheterization.
The presence of ductal calcification increases surgical risk and favours device closure.
Grade: C
Level: V
References: 45,46

Surgical closure should be reserved for those with a PDA that is too large for device closure. Examples in which the ductal anatomy may be too distorted to be acceptable for device closure include aneurysm and postendarteritis. Operative repair should probably be undertaken by congenital heart surgeons.
Grade: Consensus
References: 47,48

Part VI – Surgical/interventional outcomes

Device closure

Successful closure is achieved in the majority of attempts using a variety of devices (45,49,50). More than 85% of ducts are closed by one year following device placement. In a small proportion of patients, a second or even a third device may need to be placed. This is usually deferred for at least six months. Recanalization is rare but can occur.

Surgical closure

More than 95% of ducts can be closed by surgery. Recanalization is unusual but recognized. Postoperative complications may include recurrent laryngeal or phrenic nerve damage and thoracic duct damage.

Part VII – Pregnancy

Pregnancy is well tolerated in women with silent and small PDA, or in patients with functional class 1 or 2 before pregnancy.
Pregnancy is contraindicated in Eisenmenger syndrome because of the high maternal (up to 50%) and fetal (up to 60%) mortality.
Grade: C
Level: V
References: 22

Part VIII – Follow-up

Patients who have been repaired should have periodic evaluation by an ACHD cardiologist because recanalization can occur, or residual problems (pulmonary hypertension, left ventricular dysfunction, atrial fibrillation) may persist or develop. Patients with devices in situ should be followed up periodically because the natural history of these devices is unknown.
Endocarditis prophylaxis is recommended for six months following PDA device closure or for life if any residual defect persists.
Patients with a silent PDA do not require follow up or endocarditis prophylaxis.
Grade: Consensus

APPENDIX I
Canadian Adult Congenital Heart Network centres and contact persons

Dr Anne Williams
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APPENDIX II
Levels of evidence used in developing the management recommendations for adults with congenital heart disease

Level of evidence	Grade of recommendation
Level I: Large randomized trials with clear-cut results and low risk of error	A
Level II: Randomized trials with uncertain results and/or moderate to high risk of error	B
Level III: Nonrandomized studies with contemporaneous controls	C
Level IV: Nonrandomized studies with historical controls	C
Level V: Case series without controls	C

APPENDIX III
Types of disorders that should be seen at national or regional adult congenital heart disease centres

Aorto-left ventricular fistula
Atrioventricular septal defects
Coarctation of the aorta
Complete transposition of the great arteries
Congenitally corrected transposition of the great arteries
Coronary artery anomalies (except incidental findings)
Criss-cross heart
Cyanotic congenital heart patients (all)
Double outlet ventricle
Ebstein anomaly
Eisenmenger syndrome
Fontan procedure
Heterotaxy syndromes
Infundibular right ventricular outflow obstruction of significance
Mitral atresia
One ventricle (also called double inlet, double outlet, common, single, primitive)
Partial anomalous pulmonary venous connection
Patent ductus arteriosus (not closed)
Pulmonary atresia (all forms)
Pulmonary hypertension complicating congestive heart disease
Pulmonic valve regurgitation (moderate or greater)
Pulmonic valve stenosis (moderate to severe)
Pulmonary vascular obstructive disease
Sinus of Valsalva fistula/aneurysm
Subvalvar or supravalvar aortic stenosis
Tetralogy of Fallot
Total anomalous pulmonary venous connection
Tricuspid atresia
Truncus arteriosus or hemitruncus
Valved conduits
Ventricular septal defect with
- – Absent valves
- – Aortic regurgitation
- – Aortic coarctation
- – Mitral disease
- – Right ventricular outflow tract obstruction
- – Straddling tricuspid and/or mitral valve
- – Subaortic stenosis

APPENDIX IV
Types of diseases that may be treated exclusively in the community

Valves

- Isolated aortic valve disease
- Isolated mitral valve disease (except parachute mitral valve and similar anomalies)
- Mild pulmonic valve stenosis
- Isolated tricuspid valve disease (except Ebstein anomaly)

Shunts

- Secundum atrial septal defect (closed, no residual shunt, no arrhythmia, no pulmonary hypertension)
- Ductus arteriosus after complete closure with no residual shunt
- Ventricular septal defect (small and isolated, or repaired with no residual shunt)
- Repaired partial anomalous pulmonary venous connection

APPENDIX V
Shunts (palliative surgical interventions to increase pulmonary blood flow)

Systemic venous-to-pulmonary artery shunts

Classic Glenn	Superior vena cava to right pulmonary artery
Bidirectional Glenn	Superior vena cava to right and left pulmonary arteries
Bilateral Glenn	Right and left superior vena cava to right and left pulmonary arteries, respectively

Systemic arterial-to-pulmonary artery shunts

Classic Blalock-Taussig	Subclavian artery to ipsilateral pulmonary artery (end-to-side)
Modified Blalock-Taussig	Subclavian artery to ipsilateral pulmonary artery (prosthetic graft)
Potts' anastomosis	Descending aorta to left pulmonary artery
Waterston shunt	Ascending aorta to right pulmonary artery

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CCS Consensus Conference 2001 update: Recommendations for the Management of Adults with Congenital Heart Disease – Part II

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The Congenital Heart Disease Committee of the American College of Cardiology, the Council on Cardiovascular Disease in the Young of the American Heart Association, the Grown-Up Congenital Heart Working Group of the European Society of Cardiology, the International Society for Adult Congenital Cardiac Disease and the Japanese Society for Adult Congenital Heart Disease have all endorsed this document. Canada is fortunate to have a nationwide group of national and regional ACHD centres called the Canadian Adult Congenital Heart (CACH) Network (Appendix 1).

This material has been written in as user-friendly a fashion as possible. We envisaged a clinician looking up a lesion, and wishing to see the recommendations at a glance, rather than having to refer to other sections of the report. This has led to some repetition for the reader who begins at the beginning and ends at the end. *The repetitive portions are printed in italics to reduce frustrations resulting from this style*. We have given weight to our management recommendations.The scales that we used are shown in Appendix II. We have used standards similar to those used in past CCS Consensus Conferences.

SECTION V – LEFT VENTRICULAR OUTFLOW TRACT OBSTRUCTION

Part I – Background information

Definition: This section concerns left ventricular outflow tract obstruction (LVOTO) in the setting of concordant atrioventricular and ventriculoarterial connections. (Neither hypertrophic cardiomyopathy nor interrupted aortic arch will be considered here.)

LVOTO can occur at several levels:

- Supravalvar LVOTO may occur rarely in isolation as an hourglass deformity. It is more often diffuse, however, involving the major arteries to varying degrees, and begins at the superior margin of the sinuses of Valsalva.
- Valvar LVOTO in the adult patient with congenital heart disease is usually due to a bicuspid aortic valve (rheumatic and trileaflet calcific aortic stenosis are excluded here). It usually occurs in isolation but is associated with other abnormalities, the most common being coarctation of the aorta (which should be sought), patent ductus arteriosus (PDA) or ascending aortopathy.

This Consensus Conference on the Management of Adults with Congenital Heart Disease is an update of the previous document published in The Canadian Journal of Cardiology *1998;14:395-452. Part I was published in* The Canadian Journal of Cardiology *2001;17(9):940-959, and Part III will be published in the November issue of the* Journal

- Subvalvar LVOTO is usually either a discrete fibromuscular ridge that partially or completely encircles the left ventricular outflow tract, or a long fibromuscular narrowing beneath the base of the aortic valve. Occasionally, there is a tunnel-like narrowing of the whole left ventricular outflow tract with a small aortic root. Rarely, abnormal insertion of the mitral valve or accessory mitral leaflet may cause significant obstruction.

The concurrence of both left ventricular inflow tract obstruction (including supravalvar mitral ring, parachute mitral valve) and LVOTO (including subvalvar LVOTO, bicuspid aortic valve and aortic coarctation) is known as Shone syndrome.

Part II – Prevalence and genetics

Supravalvar LVOTO is usually part of Williams syndrome, which is a contiguous gene syndrome associated with neurodevelopmental and multisystem manifestations caused by a deletion at chromosome 7q11.23, but may be familial with normal facies, or associated with rubella syndrome.

Bicuspid aortic valve is the most common congenital cardiac anomaly occurring in 1% to 2% of the population, with a male predominance (4:1).

Subvalvar LVOTO also has a male predominance (2:1). A genetic predisposition has been suggested because there are reports of a familial incidence.

Part III – History and management of unoperated patients

Supravalvar LVOTO is usually progressive and aortic regurgitation is common. With Williams syndrome, there are often associated peripheral pulmonary artery or systemic arterial (including coronary ostial) stenoses, which may worsen, resolve or remain unchanged. Systemic hypertension is common.

Valvar LVOTO commonly progresses as the patient grows, but the rate is variable. Some patients with bicuspid aortic valve will not experience any problems, although there is a lifelong risk of endocarditis. Others will develop aortic stenosis (especially after calcification of the valve in the sixth decade), aortic regurgitation, aortic dissection or aneurysmal aortic root dilation (irrespective of altered hemodynamics or age) (1,2). If there is associated coarctation, this should usually be dealt with first (unless there is critical LVOTO; if both are severe, they may be dealt with at one operation by an anterior approach with an ascending to descending aortic graft, and concomitant aortic valve replacement).

Subvalvar LVOTO often progresses, but the rate is variable, and low gradients may remain for many years. It is often associated with aortic regurgitation (up to 60% of cases) through an otherwise normal valve that has been damaged by the subvalvar jet of blood. It may also progress, but seldom becomes more than moderate. There may be associated small ventricular septal defects (VSDs). These patients are particularly prone to endocarditis. Tunnel-like subvalvar LVOTO is progressive and requires surgery for relief of obstruction, although this may be technically difficult because the aortic root is small. Subvalvar LVOTO may occur with a variety of associated lesions.

Part IV – Diagnostic work-up

An adequate initial workup:

- Documents the level(s) of obstruction
- Quantifies the severity and anatomy of the obstruction(s)
- Identifies associated abnormalities including aortic regurgitation, proximal aortic dilation, aortic coarctation and the associated anomalies of Williams and Shone syndromes

The diagnostic workup should include at a minimum:

- *A thorough clinical assessment*
- *Electrocardiogram (ECG)*
- *Chest x-ray*
- *Transthoracic echocardiography (TTE) Doppler examination by an appropriately trained individual* to determine the level(s) of obstruction, septal thickness, and size of both the aortic root and the ascending aorta

The diagnostic workup may require:

- Transesophageal echocardiography (TEE) to define the anatomy precisely if it is unclear from TTE
- Exercise testing
- A heart catheterization with or without provocative testing to assess the hemodynamics and severity of obstruction
- Coronary angiography and aortography if surgery is being planned
- Magnetic resonance imaging (MRI) to assess associated lesions such as pulmonary artery stenoses or aortic coarctation, and to measure left ventricular mass and function
- Abdominal aortography to identify significant renal or other arterial stenoses

Part V – Indications for intervention

Supravalvar LVOTO may require intervention for a peak to peak catheterization greater than 50 mmHg, or an echocardiography peak instantaneous gradient greater than 70 mmHg, if the obstruction is discrete. Criteria for intervention for diffuse obstruction are not well defined but are probably similar because the end effect on the coronary arteries and the myocardium is the same.

Grade: C
Level: V
Reference: 3

Valvar LVOTO requires intervention for symptoms (dyspnea, angina, presyncope or syncope) or, arguably, 'critical' aortic stenosis (valve area less than 0.6 cm^2). Intervention may be indicated occasionally for other reasons (eg, a person with a lesser degree of obstruction who wishes to play vigorous sports or wishes to become pregnant). Bicuspid aortic valves may also require intervention for moderate or severe regurgitation associated with exertional symptoms, or left ventricular end systolic dimensions greater than 55 mm or left ventricular ejection fraction of less than 55%; aortic root replacement is required for ascending aortic dissection and should be considered prophylactically for proximal aortic dilation (greater than 55 mm).

Grade: C
Level: IV
References: 3-11

Subvalvar LVOTO should be considered for intervention when there is a resting catheterization peak to peak gradient greater than 50 mmHg, or echocardiography peak instantaneous gradient greater than 70 mmHg, symptoms develop, or if it is combined with progressive aortic regurgitation that is more than mild. If there is an associated VSD, the gradient may be underestimated and important subvalvar LVOTO may become manifest only after VSD closure.

Grade: C
Level: IV

Reoperation is indicated after valvotomy or after surgery for:

- Recurrent LVOTO (same criteria as above)
- Severe aortic regurgitation
- Combined restenosis with moderate or greater regurgitation, especially if symptoms or progressive left ventricular dilation is present

Grade: C
Level: IV
References: 5-8,10,18,19

Part VI – Interventional options

Patients who require operation for supravalvar LVOTO should be operated on by congenital heart surgeons with experience with the technique.

Grade: C
Level: V
References: 20,21

Supravalvar LVOTO requires patch aortoplasty or, rarely, replacement of the proximal ascending aorta.

Valvar LVOTO may be treated with the following: balloon valvuloplasty (if the valve is noncalcified); open aortic valvotomy; or valve replacement using a mechanical valve, biological valve or pulmonary autograft (Ross procedure, which consists of replacing the aortic valve with the patient's pulmonary valve and implanting a homograft in the pulmonary position). Aortic valve disease, isolated or in combination with supravalvar or subvalvar stenosis, has been increasingly treated by pulmonary autografts, especially in young adults. The choice depends on the availability and skills of the team available, and the preference of the patient.

Pulmonary autograft (Ross procedure) and balloon valvuloplasty for valvar LVOTO should be performed in centres by people with substantial experience in these procedures.

Grade: Consensus

Discrete subvalvar LVOTO requires surgical resection almost invariably associated with myomectomy or myotomy. In older patients, the aortic valve may also need to be replaced or repaired because of significant aortic regurgitation.

Tunnel-like subvalvar LVOTO may require augmentation of the LVOTO using the Konno procedure (aortoventriculoplasty with aortic valve replacement) or other modifications for enlargement of the outflow tract. In the past, a left ventricular apex-to-aorta valved conduit was implanted if it was impossible to relieve the LVOTO adequately by any other means, but the long term durability was unacceptable and the procedure has been abandoned. Some of these patients are still alive.

Subvalvar LVOTO associated with repair of atrioventricular septal defect (AVSD) often recurs if the fibromuscular tissue alone is excised. Patch enlargement of the infundibular septum and patch enlargement of the superior bridging leaflet of the left atrioventricular (mitral) valve or left atrioventricular (mitral) valve replacement may be required.

Patients who require operation for subvalvar LVOTO should be operated on by congenital heart surgeons with experience with the technique.

Grade: C
Level: V
References: 20,21

Part VII – Interventional outcomes

Supravalvar LVOTO should have a low operative mortality. Recurrence of obstruction is uncommon. The long term durability of the patches or conduits used to relieve

the obstruction may be a problem, and surveillance should include assessment for aneurysm and endocarditis.

Valvar LVOTO treated by valvotomy or valvuloplasty is associated with progressive recurrent stenosis and calcification, and/or progressive regurgitation, and may eventually require valve replacement.

Patients with subaortic stenosis who require valve replacement will have a course similar to those who have valve replacement for acquired valvar LVOTO.

Patients with pulmonary autografts have excellent hemodynamic characteristics, require no anticoagulation and have much reduced risk of thromboembolism. However, the pulmonary autograft may deteriorate with time, as may the pulmonary homograft leading to stenosis and/or regurgitation. These patients need long term follow-up.

Grade: C
Level: V
References: 22,23

Recurrence of fibromuscular subvalvar LVOTO is not uncommon (up to 20% over a decade, particularly if the aortic root is small).

Tunnel-like subvalvar LVOTO with extensive repair with or without aortic valve replacement has a high recurrence risk (24) although newer techniques may improve this risk.

Clinically important aortic regurgitation following subvalvar LVOTO repair is not uncommon (up to 25% of patients).

Part VIII – Pregnancy

LVOTO lesions associated with increased maternal and fetal risk during pregnancy include severe LVOTO with or without symptoms, aortic regurgitation and in New York Heart Association functional class III to IV, LVOTO with severe left ventricular dysfunction and mechanical prosthetic valves requiring anticoagulation. The latter underscores the importance, when feasible, of valve reconstruction or consideration of a bioprosthesis or pulmonary autograft procedure rather than replacement with a mechanical prosthesis in women having preconception cardiac surgery (25).

Patients with mild to moderate LVOTO and normal left ventricular function can usually be managed conservatively through the entire pregnancy. Patients with more severe obstruction (catheterization peak to peak gradient greater than 50 mmHg, or echocardiography peak instantaneous gradient greater than 70 mmHg before pregnancy) or symptoms should be advised to delay conception until relief of LVOTO is performed. Balloon dilation of a severely stenotic bicuspid valve during pregnancy can reduce the hazards of gestation, labour and delivery (26,27).

Aortic regurgitation with LVOTO can usually be managed medically with a combination of diuretics and/or vasodilators. Surgery during pregnancy should be contemplated only for the control of refractory functional class III or IV symptoms.

The presence of bicuspid aortic valve and ascending aortic medial abnormality may predispose patients to spontaneous aortic dissection in the third trimester.

Part IX – Follow-up

All patients should have regular cardiology follow-up. Patients with Williams or Shone syndrome, and those with complex LVOTO with or without repair should be followed up by an adult congenital heart disease (ACHD) cardiologist.

Particular attention should be paid to:

- Progressive and/or recurrent stenosis at any level
- Aortic regurgitation
- Ventricular function and/or dilation
- Aortic root dilation
- Right ventricle-pulmonary artery conduit and pulmonary autograft degeneration, (leading to neoaortic valve regurgitation) and coronary abnormalities following a Ross procedure

Endocarditis prophylaxis is recommended for prosthetic valves and for any residual lesions

Grade: Consensus

SECTION VI – COARCTATION OF THE AORTA

Part I – Background information

Coarctation of the aorta is a stenosis, usually but not always, in the region of the ligamentum arteriosum. Rarely, it can occur in the ascending or abdominal aorta. It is usually discrete but may be associated with diffuse hypoplasia of the aortic arch and isthmus. The specific anatomy, severity and degree of hypoplasia proximal to the aortic coarctation are highly variable.

Simple aortic coarctation is discrete coarctation in the absence of other intracardiac lesions. It is the most common form detected de novo in adults. 'Complex' aortic coarctation is coarctation in the presence of other important intracardiac anomalies and is usually detected in infancy. The most common associated abnormalities are VSDs, aortic stenosis, subaortic stenosis or a combination, accounting for two-thirds of cases of 'complex' aortic coarctation. The ratio of 'simple' to 'complex' aortic coarctation is approximately 1:1.

A significant aortic coarctation is usually one with right arm hypertension and a peak pull-back gradient of more than 20 mmHg across the coarctation site at angiography. If there is extensive collateral circulation, a significant aortic coarctation may have minimal or no pressure gradient, and even acquired aortic atresia.

Associated cardiovascular abnormalities include:

- Bicuspid aortic valve (up to 85%)
- Berry (intracranial) aneurysms of the circle of Willis (3% to 5%)
- Anomalies of the brachiocephalic circulation such as anomalous origin of the right subclavian artery (5%) or involvement of the left subclavian artery in the coarctation
- Collateral circulation both anteriorly (involving the internal mammary arteries) and posteriorly (involving the intercostal arteries)
- Aortic medial disease in the paracoarctation aorta, and in the ascending aorta if a bicuspid aortic valve is present
- VSD

Noncardiovascular abnormalities, involving the respiratory, gastrointestinal, genitourinary tracts or musculoskeletal system have been reported in up to 25% of cases. There is good evidence that coarctation is usually associated with a diffuse arteriopathy that persists even after repair of the coarctation itself.

Part II – Prevalence and genetics

Coarctation of the aorta is more common in men, with a male to female ratio of 1.3:1 to 1.7:1. It is usually sporadic, but genetic influences can play a role (up to 35% of Turner syndrome [45,X] females have aortic coarctation). Very rarely, it may be autosomal dominant.

Part III – History and management of unoperated patients

Presentation in adolescence and/or adulthood is usually with upper limb hypertension, differential arm-leg pulses, headaches, exertional leg fatigue or an incidental murmur. Symptoms are often absent. Rarely, presentation may be with an intracerebral hemorrhage. An occasional patient may be diagnosed from the typical x-ray appearance.

The mean survival (before widespread surgical repair and modern diagnostic methods) of patients with untreated aortic coarctation was 35 years, with 75% mortality by 46 years of age. Most developed systemic hypertension, typically during childhood, and ultimately, by the fifth decade, left ventricular failure.

Death in untreated aortic coarctation is usually due to:

- Heart failure, usually beyond 30 years of age (28%)
- Aortic rupture and/or dissection (21%)
- Infective endarteritis and/or endocarditis (18%)
- Cerebral hemorrhage (12%)
- Premature coronary artery disease
- Concomitant aortic valve disease (usually involving a bicuspid aortic valve)

Part IV – Diagnostic recommendations

An initial diagnostic workup should document:

- The location and type of aortic coarctation together with its severity
- The presence (or absence) and severity of other intracardiac lesions (bicuspid aortic valve, mitral valve abnormalities, subaortic stenosis, VSD)
- Left ventricular function and the presence (or absence) of left ventricular hypertrophy
- The presence (or absence) of other extracardiac cardiovascular anomalies such as collateral circulation, involvement of other vessels (subclavian and/or carotid stenoses) and associated aneurysms

The diagnostic workup should include at a minimum:

- *a thorough clinical assessment*, including upper and lower limb blood pressure measurement, determination of radiofemoral pulse delay, palpation of femoral and distal pulses, and auscultation for collaterals around the scapula
- *ECG*, which may show signs of left ventricular hypertrophy with more or less 'strain'
- *Chest x-ray*, which may show the 'three sign' (caused by indentation of the aorta at the site of the aortic coarctation, combined with dilation before and after the coarctation) or 'rib notching' (caused by erosion of the inferior border of the posterior ribs by enlarged intercostal arteries)
- *Echocardiography Doppler evaluation by an appropriately trained individual*. The echocardiography window, in particular, the suprasternal arch view, may be difficult in adults
- MRI to delineate the coarctation anatomy, possible aneurysm formation and with velocity mapping, assess the degree of restenosis. Contrast magnetic resonance angiography may allow visualization of arch geometry and collaterals (28)

The diagnostic workup may require:

- Invasive angiography with hemodynamic measurements to assess the aortic coarctation gradient and nature of the obstruction, and to determine the presence and/or absence of collaterals or aneurysm formation if appropriate information cannot be obtained by MRI, if MRI is not available or if percutaneous intervention is not planned. If percutaneous intervention is planned, angiography can be performed at the time of procedure
- Digital subtraction angiography (DSA), which provides good anatomical detail and may obviate the need for invasive arteriography

- Complete heart catheterization with aortography if associated cardiovascular lesions are present
- Coronary angiography because of the increased risk of premature coronary artery in these patients, if a clinical indication exists, if the patient is over 40 years of age (or younger if major coronary risk factors) or if there is any evidence of left ventricular failure

Part V – Indications for intervention

All patients with significant aortic coarctation or recoarctation, including those with proximal systemic hypertension (regardless of age) whether symptomatic or asymptomatic, warrant intervention.

Grade: C
Level: V
Reference: 29

Patients with significant aortic valve stenosis may also require valve surgery, which may or may not be done at the same time as aortic coarctation repair. If operated on separately, the sequence depends on the severity of each of the lesions, the more severe one being dealt with first.

Part VI – Surgical and/or interventional options

For aortic coarctation or recoarctation, intervention may be either surgical or percutaneous (30). Surgical repair remains the gold standard against which newer therapies must be compared.

Surgical repair of aortic coarctation in adults is more hazardous than in children. It should be performed by congenital heart surgeons.

Grade: C
Level: V
References: 20,21

Surgical repair may involve:

- Interposition graft
- End-to-end anastomosis (usually the preferred method for initial repair)
- Patch aortoplasty
- Arch augmentation
- Jump graft bypassing the aortic coarctation segment
- Subclavian flap aortoplasty (may be used in children but not recommended in adults because of concern about the arterial supply to the arm)

Balloon dilation and/or stent insertion is being used increasingly as an alternative to surgery and, in some centres, has replaced surgery as the primary management strategy, unless additional problems coexist. It is not an appropriate therapy if there is an interposition graft or important concomitant arch hypoplasia involving the origin of the left common carotid or in the proximal arch. It should only be performed in centres and by people with a commitment to the technique and to its clinical evaluation.

Grade: Consensus
References: 31,32

If there is aortic stenosis, and the aortic coarctation is relieved first, re-evaluation of the aortic gradient is needed after the procedure. This is usually accomplished with echocardiography Doppler.

Part VII – Surgical/interventional outcomes

Following surgical repair of simple aortic coarctation, the obstruction is usually relieved with minimal mortality (less than 1%). Mortality is higher for reoperation (5% to 15%). Recurrent coarctation is more common when initially repaired in infancy.

Complications of surgical repair include:

- Paraplegia due to spinal cord ischemia. It is uncommon but recognized, particularly in patients who do not have well developed collateral circulation
- Rebound paradoxical hypertension in the early postoperative phase. It may be due to rebound sympathetic activation and activation of the renin-angiotensin system. It usually responds to beta blockade
- Recurrent laryngeal nerve palsy
- Phrenic nerve injury with diaphragmatic paralysis
- Aneurysm formation following patch aortoplasty (particularly Dacron). It occurs opposite the patch
- Late dissection at the repair site is a rare complication, but false aneurysms may occur
- Arm claudication (rare) if subclavian flap aortoplasty has been used

Balloon dilation and/or intravascular stenting for native aortic coarctation or recoarctation can be as effective as surgical repair in relieving stenoses, with similar mortality (33-35). The long term outcomes are unknown.

The complications of balloon dilation and/or intravascular stenting include:

- Recoarctation. The rate is higher for balloon dilation without stenting compared with surgery, particularly for younger patients
- Aneurysm formation (6% to 12% with native aortic coarctation), although this is substantially less with stent use
- Femoral artery injury and/or thrombosis
- Stroke (rare)
- Aortic rupture (rare)

Hemoptysis from a leaking and/or ruptured aneurysm is a life-threatening complication and requires immediate investigation and treatment. MRI or DSA are optimal because of the risk of rupture with aortography and also, at times, failure to visualize the aneurysm.

Long term follow-up after surgical repair has shown an increased incidence of premature cardiovascular disease and death (36).

Prior hypertension resolves in many patients, but this may depend on the length of follow-up and age at repair. If hypertension fails to resolve, it is generally responsive to standard therapy. Systolic hypertension is common with exercise, the significance of which is unknown. It may be related to residual arch hypoplasia. Persistent exercise-induced upper limb hypertension may occur, even in the absence of any significant residual gradient.

Heart failure usually resolves.

Late strokes may occur, notably in patients repaired as adults and in those with residual hypertension. Cerebral hemorrhage due to a ruptured berry aneurysm can occur late after repair, even in the absence of systemic hypertension.

Endocarditis and/or endarteritis can occur at the aortic coarctation site or involving associated lesions. If it is at the coarctation site, embolic manifestations are usually restricted to the abdominal viscera and legs.

Part VIII – Pregnancy

Women with aortic coarctation contemplating pregnancy should have repair before pregnancy. The management of hypertension in the unoperated pregnant patient may be problematic because too low a pressure below the coarctation site may result in abortion or death of the fetus. The risk of aortic dissection or aneurysm rupture during pregnancy is low, but death is likely if one of these occurs.

Grade: C
Level: V
References: 37-40

Part IX – Follow-up

All patients require periodic follow-up by an ACHD cardiologist.

All patients should have a periodic MRI or angiogram following repair of the aortic coarctation to document the postrepair anatomy and mechanical complications (restenosis or aneurysm formation).

Particular attention should be directed toward:

- Residual hypertension, heart failure, coronary artery disease or other cardiac disease
- Associated bicuspid aortic valve, which may develop stenosis or regurgitation later in life
- Recurrent aortic coarctation or significant arm-leg blood pressure gradient at rest
- Ascending aortopathy, especially in the presence of bicuspid aortic valve
- New or unusual headaches because of the possibility of berry aneurysms
- Late dissection proximal or distal to the repair site
- Aneurysm formation at the site of aortic coarctation repair, especially if either a Dacron patch or if balloon angioplasty has been used

Endocarditis prophylaxis is recommended for six months following coarctation repair or for life if any residual gradient or associated indications persist.

Grade: Consensus

SECTION VII – RIGHT VENTRICULAR OUTFLOW TRACT OBSTRUCTION

Part I – Background information

Supravalvar right ventricular outflow tract (RVOT) obstruction seldom occurs in isolation. It may occur in tetralogy of Fallot, Williams syndrome, Noonan syndrome, VSD, arteriohepatic dysplasia or congenital Rubella syndrome.

Valvar RVOTO, the most common form of RVOTO, is almost always congenital in origin. Typically, the stenotic pulmonic valve is a thin, pliable, dome-shaped structure, with a narrow opening at its apex. In 10% to 15% of cases, the valve is dysplastic with thickened and immobile cusps. In adults, the valve may calcify late in life.

Subvalvar (infundibular) RVOTO usually occurs in combination with other lesions, particularly VSD, and as part of tetralogy of Fallot.

A separate but somewhat similar entity is 'double-chambered right ventricle' with midcavity obstruction,

often from a prominent moderator band. This may be associated with a VSD.

RVOTO (either valvar or subvalvar) may rarely occur in association with subaortic stenosis.

Branch pulmonary artery stenosis is not considered here.

Hemodynamic severity grading

The following is based on peak systolic pressure gradients at heart catheterization). It is time-honoured and useful for decisions regarding therapy.

Trivial:	less than 25 mmHg
Mild:	25 to 49 mmHg
Moderate:	50 to 79 mmHg
Severe or critical:	greater than 80 mmHg

Part II – Prevalence and genetics

Patients with Noonan syndrome (autosomal dominant inheritance) may present with pulmonary stenosis, atrial septal defect (ASD) and restrictive cardiomyopathy. Mental retardation, abnormal facies, short stature, thoracic/penile and/or testicular abnormalities may also be present. Williams syndrome is a contiguous gene syndrome associated with cardiac (pulmonary stenosis, pulmonary artery stenosis, supravalvar aortic stenosis), neurodevelopmental (mental retardation, 'cocktail personality') and multisystem manifestations (abnormal facies, short stature, hypercalcemia) caused by a deletion at chromosome 7q11.23. Patients with Alagille syndrome (autosomal dominant inheritance – also called arteriohepatic dysplasia) may have pulmonary stenosis, pulmonary arterial stenosis and abnormal facies (prominent overhanging forehead, deep-set eyes, small pointed chin).

Part III – History and management of unoperated patients

Supravalvar RVOTO may progress in severity and should be monitored.

Patients with trivial valvar RVOTO who are asymptomatic do not become worse with time as adults and will not require treatment, unless endocarditis occurs.

Grade: C
Level: IV
Reference: 41

Female patients often present to physicians during pregnancy because of an increase in the loudness of the murmur. Others may present because of enlarged pulmonary arteries detected on chest x-ray.

Mild valvar RVOTO may progress in 20% of unoperated patients. Moderate stenosis may progress in up to 70% of unoperated patients. Some of these patients will also become symptomatic later in life because of atrial arrhythmias. When the gradient is moderate to severe or the patient is symptomatic, balloon valvotomy (or rarely surgical valvotomy) is recommended.

Grade: C
Level: IV
References: 41,42

Subvalvar RVOTO usually progresses in severity and often leads to the development of worsening right ventricular hypertrophy, symptoms and critical gradients requiring surgical repair.

Part IV – Diagnostic work-up

An adequate diagnostic workup:

- Documents the level(s) of obstruction
- Quantifies the severity of the obstruction(s)
- Identifies associated abnormalities such as ASD, PDA, VSD and tetralogy of Fallot

The diagnostic workup should include at a minimum:

- A *thorough clinical assessment*, paying particular attention to the 'a' wave on the venous pulse, the length of the murmur, and the pulmonary component of the second sound and right ventricular hypertrophy
- *ECG*
- *Chest x-ray*, paying particular attention to valvar calcification on the lateral film
- *Echocardiography Doppler examination by an appropriately trained individual*

The diagnostic workup may require:

- Oximetry (rest and exercise) to determine whether there is cyanosis because of associated abnormalities (ASD or VSD)
- Heart catheterization (including angiocardiography) to assess the hemodynamics and severity of obstruction, and pulmonary artery abnormalities
- *Coronary angiography in patients at risk of coronary artery disease, or in patients over the age of 40 years in whom intervention is being planned*
- MRI to assess associated lesions such as pulmonary artery stenoses, coexisting pulmonary regurgitation and right ventricular function if unable to assess these properly by echocardiography or angiogram

Part V – Indications for intervention and/or reintervention

Intervention is indicated if:

- The combined pullback peak to peak gradient at catheterization across the RVOT is greater than 50 mmHg at rest
- Symptoms are present (exertional dyspnea, angina, presyncope or syncope)

Grade: C
Level: IV
Reference: 43

Intervention is also indicated if:

- There are important arrhythmias (usually sustained atrial flutter)
- There is an associated ASD or VSD, especially if there is right-to-left shunting
- There is a double-chambered right ventricle with significant midcavity obstruction (pullback peak to peak gradient at catheterization greater than 50 mmHg)

Grade: Consensus
Reference: 43

Intervention may be indicated following an episode of endocarditis.

Reintervention is indicated for:

- Recurrent RVOTO after prior surgery or balloon valvotomy (same criteria as above)
- Severe pulmonic regurgitation associated with reduced exercise capacity of cardiovascular cause or deteriorating right ventricular function, or substantial tricuspid regurgitation or sustained atrial flutter and/or fibrillation or sustained ventricular tachycardia

Grade: C
Level: V
Reference: 44

Part VI – Surgical/interventional options

Balloon valvuloplasty is the treatment of choice for valvar RVOTO. Occasionally, valve replacement may be necessary.

Grade: C
Level: IV
References: 45,46

Balloon valvuloplasty for valvar RVOTO is an established technique but should still be performed only in centres and by teams with experience in this technique.

Grade: Consensus
References: 45,46

Relief of obstruction in a double-chambered right ventricle is accomplished by surgical resection of right ventricular muscle bands.

Patients who require operation for supravalvar or subvalvar RVOTO should be operated on by congenital heart surgeons.

Grade: C
Level: V
References: 20,21

Part VII – Surgical and/or interventional outcomes

The long term results of surgical pulmonary valvotomy are established. Clinical outcomes are excellent. Relief of valvar RVOTO is usually maintained, but residual obstruction may progress. Occasionally, pulmonary regurgitation may progress and become severe enough to warrant reintervention. Long term survival in surgical patients is close to normal when valvar RVOTO occurs as an isolated lesion. Long term mortality may be increased, however, with greater age (greater than 21 years) at the time of surgery.

Patients treated with balloon valvuloplasty, in the absence of a dysplastic valve, have the same prognosis as those who have had surgical valvotomy, at least in the medium term (47,48).

Subvalvar and supravalvar RVOTO seldom recur after adequate repair.

Part VIII – Pregnancy

The increased hemodynamic load of pregnancy may precipitate right heart failure, atrial arrhythmias or tricuspid regurgitation in patients with significant RVOTO, irrespective of the presence or absence of symptoms before pregnancy. Patients with moderate to severe RVOTO should, therefore, be considered for RVOTO relief before conception.

Balloon valvuloplasty for valvar pulmonary stenosis may be employed during pregnancy if the stenosis is severe or symptoms due to pulmonary stenosis develop. When possible, intervention should be delayed until after organogenesis.

Mild RVOTO or RVOTO that has been alleviated by valvuloplasty or surgery (with or without pulmonary regurgitation) is well tolerated.

Part IX – Follow-up

Patients with trivial RVOTO (gradient less than 25 mmHg) do not require ACHD cardiology follow-up. Follow-up by a general physician and/or internist/cardiologist is sufficient unless new findings or symptoms occur.

Patients with mild or greater RVOTO, or moderate to severe pulmonary regurgitation, require monitoring by an ACHD cardiologist because intervention may be required.

Particular attention should be paid to:

- Progressive and/or recurrent stenosis, especially at the subvalvar level
- Right ventricular size and function in the context of significant pulmonary/subpulmonary stenosis and/or regurgitation
- Tricuspid regurgitation (often reflecting right ventricular dysfunction)
- Atrial and occasionally ventricular (usually postoperative) arrhythmias (sustained)
- Evidence of intracardiac shunting, especially right-to-left

Endocarditis prophylaxis is recommended.

Grade: Consensus

SECTION VIII – TETRALOGY OF FALLOT

Part I – Background information

Definition: Tetralogy of Fallot is due to the following: anterocephalad deviation of the outlet septum resulting in an unrestricted large anterior malalignment subaortic VSD; RVOTO, which may be infundibular, valvar, supravalvar or a combination of all; consequent right ventricular hypertrophy; and an overriding aorta (less than 50%). Accompanying features can include additional muscular VSDs, anomalous coronary arteries, a right-sided aortic arch, PDA, aortic root dilation and aortopulmonary collaterals (mainly seen in patients with pulmonary atresia and/or VSD, which is not discussed here).

The so-called pentalogy of Fallot also has an ASD or patent foramen ovale (PFO).

Part II – Prevalence and genetics

Approximately 15% of patients with tetralogy of Fallot have a deletion of chromosome 22q11 (49).The incidence is especially high in patients with right aortic arch, pulmonary atresia and aortic-to-pulmonary collaterals. The clinical spectrum is summarized in the 22q11 deletion syndrome (cardiac defect, abnormal facies, thymic hypoplasia, cleft palate, hypocalcemia and 22q11 deletion). These patients may have an elevated risk of late psychiatric disorders. Deletion of 22q11 is usually sporadic. Affected subjects, however, have a 50% risk (autosomal dominant) of transmitting the deletion to their offspring.

Part III – History and management of unoperated patients

The pathophysiology varies depending on the degree of RVOTO.

With relatively mild obstruction, the presentation is of increased pulmonary blood flow and minimal cyanosis, so-called 'pink tetralogy' or 'acyanotic Fallot'. This occasionally presents in adulthood.

Most children, however, have significant RVOTO with consequent right-to-left shunt and cyanosis. Most of them will have had reparative surgery.

Rarely, adults present who are unoperated. For them, surgical repair is still recommended because the results are gratifying and the operative risk is comparable with pediatric series (provided there is good left ventricular function and no serious coexisting morbidity) (50,51).

Some patients reach adulthood with previous palliation only. The types of palliative procedures include:

- Blalock-Taussig shunt or modification (subclavian artery-to-pulmonary artery shunt)
- Waterston shunt (ascending aorta-to-right pulmonary artery)
- Potts shunt (descending aorta-to-left pulmonary artery)
- Central interposition tube graft
- Infundibular resection (Brock procedure) or pulmonary valvotomy
- Right ventricular to pulmonary artery conduit without VSD closure or with fenestrated closure

Reparative surgery involves closing the VSD and relieving the RVOT obstruction. The latter may involve:

- Resection of infundibular muscle
- Right ventricular subannular outflow tract patch
- Transannular patch (a patch across the pulmonary valve annulus that disrupts the integrity of the pulmonary valve and causes substantial pulmonary regurgitation)
- An extracardiac conduit placed between the right ventricle and pulmonary artery (in cases of anomalous coronary artery crossing the RVOT)
- Replacement of the pulmonary valve
- Pulmonary valvotomy
- Pulmonary arterioplasty

A PFO or secundum ASD should be closed, and an AVSD repaired, if present.

Additional lesions such as aortic regurgitation or muscular VSDs may also need to be addressed.

Part IV – Investigational recommendations in operated patients

Investigations are directed toward the postoperative sequelae and vary according to the type of operation performed.

All patients should have, at a minimum:

- *A thorough clinical assessment*
- *ECG*
- *Chest x-ray*
- *Echocardiography Doppler examination by an appropriately trained individual* to detect and quantify residual pulmonary stenosis and regurgitation, residual VSD, right and left ventricular size and function, aortic regurgitation and aortic root size

Patients may require:

- Exercise testing to assess functional capacity and to evaluate possible exertional arrhythmias
- Holter monitoring
- Quantitative lung perfusion scan in patients with suspected pulmonary artery branch stenosis
- Heart catheterization if adequate assessment of the hemodynamics is not obtainable by noninvasive means, including pulmonary angiography in patients with suspected pulmonary artery branch stenosis and coronary angiography if surgical reintervention is planned
- Electrophysiology study for those being evaluated because of sustained atrial flutter or fibrillation, or for sustained monomorphic ventricular tachycardia or fibrillation
- MRI for the assessment of pulmonary artery or aortic anomalies, pulmonary regurgitant fraction, as well as right ventricular size and function

For patients who have had previous palliation, assessment of pulmonary artery pressure and anatomy is mandatory at some point, because these shunts have inherent complications (distortion of the pulmonary arteries, stenosis or aneurysm in the shunt or at the site of anastomosis, development of pulmonary hypertension, and volume overloading of the left heart).

The following issues may need to be addressed after a palliative shunt:

- Determine whether complete repair is possible
- Explain increasing cyanosis with erythrocytosis
- Determine whether pulmonary hypertension is present (unilateral or bilateral)
- Explain the reduction or absence of the continuous shunt murmur (suspected shunt stenosis, occlusion or pulmonary hypertension)
- Determine whether there is aneurysm formation in the shunt

Patients presenting as adults who have not been repaired may have elevated pulmonary artery pressures despite severe RVOT obstruction.

Part V – Indications for reintervention

Following palliative surgery, complete intracardiac repair should be considered in all patients in the absence of severe irreversible pulmonary hypertension or unfavourable anatomy (inadequate pulmonary arteries). The following situations particularly warrant complete repair:

- Worsening symptoms
- Increasing cyanosis with erythrocytosis
- Reduction or absence of the continuous shunt murmur (suspected shunt stenosis, occlusion or pulmonary hypertension)
- Aneurysm formation in the shunt
- Left ventricular dilation in the presence of aortic regurgitation or a left-to-right shunt

Grade: Consensus
Reference: 51

Reoperation is only necessary in approximately 10% to 15% of patients following reparative surgery over a 20-year follow up.

The following situations may warrant intervention following repair:

- Residual VSD with a shunt greater than 1.5:1
- Residual pulmonary stenosis with right ventricular pressure two-thirds of systemic pressure or more (either the native right ventricular outflow or valved conduit if one is present)
- Free pulmonary regurgitation associated with progressive or moderate to severe right ventricular enlargement, important tricuspid regurgitation, sustained atrial or ventricular arrhythmias, or symptoms such as deteriorating exercise performance
- Significant aortic regurgitation associated with symptoms and/or progressive left ventricular systolic dysfunction
- Aortic root enlargement 55 mm in diameter or more
- A large RVOT aneurysm, or evidence of infection or false aneurysm
- Sustained clinical arrhythmias, most commonly either atrial flutter or fibrillation, or sustained monomorphic ventricular tachycardia. When any of these arrhythmias occur, a treatable cause of hemodynamic deterioration should be sought
- The combination of residual VSD, and/or residual pulmonary stenosis and regurgitation, all mild to moderate but leading to progressive right ventricular enlargement, reduced right ventricular enlargement function or symptoms

Grade: C
Level: V
References: 44, 52-58

Part VI – Surgical and/or interventional options

Patients who require intervention should be operated on by congenital heart surgeons.

Grade: C
Level: V
References: 20,21

The following are possible intervention strategies:

- Surgery may be necessary for residual pulmonary stenosis; this may involve resection of residual infundibular stenosis or placement of a right ventricular outflow or transannular patch. Occasionally, a valved extracardiac conduit may be necessary
- Aortic valve and/or root replacement may be necessary for those with aortic valve regurgitation and/or root dilation
- Reoperation to insert a new pulmonary valve (either homograft or porcine) may be necessary for severe pulmonary regurgitation leading to right ventricular dilation, sustained arrhythmias and/or symptoms. Tricuspid valve (TV) annuloplasty may also be necessary when at least moderate tricuspid regurgitation is present
- Suture or patch closure of a residual VSD if the shunt is 1.5:1 or more, or if the patient is undergoing cardiac reoperation for other reasons
- Branch pulmonary artery stenosis may be managed with balloon dilation with or without stent insertion or surgery
- Radiofrequency or surgical cryoablation for atrial flutter and sustained ventricular tachycardia. Maze procedure including pulmonary vein encirclement for atrial fibrillation
- The role of automatic implantable cardioverter-defibrillator (AICD) for arrhythmias in these patients is unclear
- Closure of ASD or PFO, especially if there is persistent cyanosis or paradoxical embolus

Part VII – Surgical/interventional outcomes

The overall survival of patients who have had operative repair is excellent, provided that the VSD has been closed and the RVOTO has been relieved. A 36-year survival rate of 85% has been reported (59). Death may occur from reoperation, endocarditis or congestive heart failure. The cumulative risk of sudden death following repair of tetralogy of Fallot seems to be about 1.2% at 10 years, 2.2% at 20 years, 4% at 25 years and 6% at 35 years (accounting for approximately one-third of late deaths) (59,60).

Pulmonary valve replacement for chronic significant pulmonary regurgitation can be performed with a low mortality and may lead to improvement in right ventricular dimension and performance if completed before marked right ventricular dysfunction supervenes (58,61).

Part VIII – Arrhythmias

Whereas nonsustained ventricular arrhythmia on Holter is common, sustained monomorphic ventricular tachycardia is relatively uncommon. The latter relates to abnormal hemodynamics, usually from right ventricular dilation secondary to pulmonary regurgitation and/or tricuspid regurgitation. QRS duration on the surface ECG correlates to right ventricular size and when prolonged (QRS 180 ms or greater) is a sensitive (although less specific) predictor of sustained ventricular tachycardia and sudden death (62).

Restoration of hemodynamics through pulmonary valve implantation, TV repair, or RVOT aneurysm resection, with concomitant intraoperative cryoablation, has a positive effect on pre-existing sustained ventricular tachycardia (58,63). There is clearly a role for antiarrhythmic drugs, but addressing the underlying hemodynamics is usually the top priority. AICD implantation may also have a role for secondary prevention of sudden death; particularly so for patients with advanced ventricular dysfunction, nonresponsive to reoperations or without hemodynamic abnormalities amenable to surgery.

Atrial flutter and fibrillation occur in one-third of the adult patients and contribute to morbidity and even late mortality (64). As with sustained ventricular tachycardia, restoration of acceptable hemodynamics with concomitant cryoablation and antiarrhythmic medication are the main therapeutic tools (58,63).

Part IX – Pregnancy

Pregnancy in unoperated patients constitutes a considerable risk of maternal and fetal complications and death. This risk is greater when resting oxygen saturations are less than 85%. The fall in peripheral resistance during pregnancy, and hypotension during labour and delivery may increase the right-to-left shunt and aggravate pre-existing cyanosis.

The risk of pregnancy in repaired patients depends on the hemodynamic status. The risk is low, approaching that of the general population, in patients with good underlying hemodynamics. In patients with significant residual RVOTO, severe pulmonary regurgitation with or without tricuspid regurgitation and right ventricular dysfunction, the increased volume load of pregnancy may lead to right heart failure and arrhythmias.

All patients with tetralogy should have cardiology counselling preconception and follow-up by an ACHD cardiologist during pregnancy. Preconception assessment of 22q11 deletion syndrome using fluorescent in situ hybridization (FISH) is recommended.

Part X – Follow-up

All tetralogy patients should have regular cardiology follow-up by an ACHD cardiologist.
Endocarditis prophylaxis is recommended.

Grade: Consensus

SECTION IX – EBSTEIN ANOMALY

Part I – Background information

Ebstein anomaly is rare. The term encompasses a wide spectrum of anatomical and functional abnormalities of the morphological TV, which have certain features in common:

- Apical displacement of the septal and posterolateral leaflets of the TV below the atrioventricular junction into the right ventricle
- Resultant 'atrialization' of the inflow of the right ventricle to varying degrees and consequently a smaller 'functional' right ventricle
- Varying degrees of tricuspid regurgitation (exceptionally, the TV is stenotic)
- Enlargement of the right atrium
- A shunt at atrial level, either PFO or secundum ASD, in approximately 50%
- One or more accessory conduction pathways, increasing the risk of atrial tachycardias, in 25% of patients
- Varying degrees of anatomical and physiological right ventricular inflow or outflow tract obstruction
- Varying impairment of left ventricular function (65-67)
- Varying degrees of cyanosis (less than half of patients)

Associated lesions may include:

- VSD
- Pulmonary stenosis
- Occasionally others, such as aortic coarctation or mitral valve prolapse

Part II – History and management of unoperated patients

Patients with mild Ebstein anomaly may be asymptomatic with no functional limitation. Survival to the ninth decade has been reported. Patients with moderate Ebstein anomaly may become symptomatic during late adolescence or young adult life. Patients with severe Ebstein usually present at birth or even in utero.

The most common symptoms in adults are exercise intolerance (dyspnea and fatigue) and symptomatic supraventricular arrhythmias. Heart block occasionally occurs.

When an atrial defect is present, patients may be cyanotic (to a varying degree – particularly during exercise), and are at risk of a paradoxical embolus resulting in transient ischemic attack and/or stroke. Alternatively, they may have a left-to-right shunt at rest, which can reverse on effort.

End-stage disease with severe tricuspid regurgitation and right ventricular dysfunction may manifest as right-sided cardiac failure. It is usually precipitated by an arrhythmia such as atrial flutter or fibrillation. Sudden death (presumed arrhythmic in nature) may occur at any age and is more likely if accessory pathway(s) is/are present (68-74).

Part III – Diagnostic work-up

An adequate diagnostic workup:

- Documents the anatomical severity (degree of apical displacement of the TV) with resultant degree of right-sided enlargement, right ventricular dysfunction and degree of tricuspid regurgitation
- Determines whether the TV has the potential for surgical repair. This depends on the anterior leaflet size and degree of tethering, as well as the relative size of the 'functional' right ventricle
- Documents the presence or absence of an atrial communication, and whether there is right-to-left shunting
- Determines the presence or absence of associated lesions
- Measures left ventricular function and identifies any mitral valve abnormalities
- Defines, if possible, the presence or absence of an accessory pathway
- Determines the amount of functional limitation, if any

The initial workup should include at a minimum:

- *A thorough clinical assessment*
- *ECG*
- *Chest x-ray*
- *Echocardiography Doppler evaluation by an appropriately trained individual*
- Oximetry

The diagnostic workup may require:

- Exercise test
- TEE Doppler examination if the anatomical information is not provided by TTE
- Holter monitor
- An electrophysiological study if there is a history or ECG evidence of arrhythmias or accessory pathway(s)
- *Coronary angiography in patients at risk of coronary artery disease or in patients over the age of 40 years if surgical repair is planned*

Part IV – Indications for intervention

The following situations warrant intervention:

- Deteriorating exercise capacity (New York Heart Association class greater than II)
- Increasing heart size (**cardiothoracic ratio** greater than 60%)
- Important cyanosis (resting oxygen saturation less than 90%)
- Severe tricuspid regurgitation with symptoms
- A transient ischemic attack or stroke
- Sustained atrial flutter or fibrillation
- Atrial arrhythmias secondary to an accessory pathway

Grade: C
Level: V
References: 75,76

Part V – Interventional options

Ebstein anomaly should only be repaired by congenital heart surgeons, ideally those with substantial specific experience in this operation. Every effort should be made to preserve the native TV.

Grade: C
Level: V
References: 77-81

When the anterior TV leaflet is mobile and can serve as a monocusp valve, and the functional right ventricle is of adequate size (greater than one-third of the total right ventricle), valve repair may be possible and is preferable to valve replacement (82).

If the TV is not repairable, valve replacement is necessary.

An atrial communication, if present, should be closed.

Given normal pulmonary artery pressures, in patients with an inadequate right ventricle (because of size or function), severe tricuspid regurgitation and chronic supraventricular arrhythmias, a bidirectional cavopulmonary connection may be used to supplement the intracardiac repair.

Occasionally, a Fontan operation may be the best option in patients with tricuspid stenosis and/or hypoplastic right ventricle.

It is controversial whether the atrialized portion of the right ventricle should be plicated to improve hemodynamics and reduce the risk of atrial arrhythmias. Radiofrequency or operative cryoablation have been successful in preventing atrial flutter. A maze procedure, including pulmonary vein encirclement, may be helpful to prevent and treat atrial fibrillation.

Part VI – Interventional outcomes

With satisfactory valve repair, with or without bidirectional cavopulmonary connection, medium term prognosis is excellent. Late arrhythmias, most commonly atrial tachyarrhythmias and seldom complete atrioventricular block, may occur (83,84).

Valve rereplacement may be necessary because of a failing bioprosthesis or thrombosed mechanical valve. There is a high incidence of complete heart block with TV rereplacement.

Part VII – Arrhythmias

In patients with chronic supraventricular arrhythmias (atrial fibrillation and/or flutter), concomitant cryoablation and/or right atrial maze procedure at the time of surgery may be considered (80). Radiofrequency ablation is less successful because of the commonly very large right atrium.

If an accessory pathway is present, this should be mapped and can be obliterated either at the time of surgical repair or preoperatively in the catheter laboratory (85). However, multiple pathways are common, and preoperative ablation may prove to be difficult.

Part VIII – Pregnancy

In the absence of maternal cyanosis, right-sided heart failure or arrhythmias, pregnancy is usually well tolerated (86,87).

Part IX – Follow up

All Ebstein patients should have regular follow-up with an ACHD cardiologist. Particular attention should be paid to:

- Cyanotic patients
- Substantial cardiomegaly (cardiothoracic ratio greater than 60%)
- Right-sided ventricular function, which may worsen and cause congestion
- Tricuspid regurgitation or tricuspid stenosis in the previously operated patient
- Degeneration and/or infection of a bioprosthetic valve or thrombosis and/or infection of the mechanical valve
- Recurrent atrial arrhythmias
- Ventricular arrhythmias
- Complete heart block

Endocarditis prophylaxis is recommended for six months following Ebstein repair or for life if any residual gradient and/or lesions persist or in the presence of a prosthetic valve.

Grade: Consensus

SECTION X – MARFAN SYNDROME

Part I – Background information

Definition: Marfan syndrome is an autosomal dominantly inherited disorder of connective tissue in which cardiovascular, skeletal, ocular and other abnormalities may be present to a highly variable degree. The prevalence has been estimated to be one in 3000 to one in 5000.

Part II – Prevalence and genetics

New mutations account for 25% to 30% of cases of Marfan syndrome. The clinical features are the result of a weakening of the supporting tissues, due to defects in fibrillin-1, a glycoprotein and a principal component of the extracellular matrix microfibril. The gene for fibrillin-1 (*fbn*1) is located on chromosome 15. More than 200 mutations in *fbn*1 have been described. The phenotype presents to a highly variable degree due to varying genotype expression (88-90).

Part III – History and management of unoperated patients

The prognosis of patients with Marfan syndrome is mainly determined by aortic root abnormalities, which predispose the aorta to progressive dilation and dissection, and lead to aortic regurgitation. The mean survival of untreated patients is 40 years, but the variance is large. Not only the aortic root, but also other parts of the aorta and 'elastic' arteries may be dilated, and may dissect or rupture, although much less commonly. Patients with a dilated aorta are usually asymptomatic. The presence of aortic regurgitation or mitral valve prolapse with regurgitation may lead to signs or symptoms of left ventricular volume overload.

Both medical and surgical therapies have improved life expectancy substantially, from a mean survival of 40 years in 1972 (91) to approximately 60 years in 1993 (92). The risk of type A dissection clearly increases with increasing aortic root diameter. Nonetheless, aortas with no or only mild dilation occasionally dissect. A beneficial effect of beta-adrenergic blockade has been shown in slowing the rate of aortic dilation and reducing the risk of dissection (93,94).

To reduce aortic and arterial stress, the use of beta-blockade is recommended, as well as the avoidance of maximal and isometric exertion, and contact sports.

Grade: C
Level : V
References: 93,94

Part IV – Diagnostic work-up

An adequate diagnostic workup:

- Documents the basis for the diagnosis of Marfan syndrome, using the 'Ghent criteria' (95) (Table 1)
- Determines the diameter and searches for dissection of the aortic root and all other parts of the aorta
- Determines whether aortic regurgitation is present
- Determines the presence of mitral valve prolapse, mitral regurgitation, calcification of the mitral annulus, presence of TV prolapse, tricuspid regurgitation and the diameter of the main pulmonary artery

The accuracy of diagnosis is critical and requires a rigorous approach. To this point, the diagnosis of Marfan syndrome is made on clinical grounds. Because of the variability in clinical expression, a multidisciplinary evaluation in a centre for Marfan screening is recommended for a complete evaluation of a patient and for screening of the patient's relatives for Marfan syndrome.

A definite diagnosis requires occurrence of major manifestations in two different categories, and involvement (presence of criteria) of a third category (Table 1).

Grade: Consensus
References: 95

TABLE 1
Diagnostic criteria for Marfan syndrome

Criteria	Major	Minor
Family history	Independent diagnosis in parent, child, sibling	None
Genetics	Mutation *fbn*1	None
Cardiovascular	Aortic root dilation; dissection of ascending aorta	Mitral valve prolapse; calcification of the mitral valve (<40 years); Dilation of the pulmonary artery; Dilation/dissection of the descending aorta
Ocular	Ectopia lentis	Two needed – flat cornea, myopia, elongated globe
Skeletal (reference 101)	Four needed – pectus excavatum needing surgery, pectus carinatum, pes planus, wrist and thumb sign, scoliosis >20° or spondylolisthesis, arm span-height ratio >1.05, protrusio acetabulae (x-ray, MRI), diminished extension elbows (<170°)	Two to three major, or one major and two minor signs – Moderate pectus excavatum; High, narrowly arched palate; Typical facies; joint hypermobility
Pulmonary		Spontaneous pneumothorax; apical bulla
Skin		Unexplained stretch marks (striae); Recurrent or incisional herniae
Central nervous system (references 101,102)	Lumbosacral dural ectasia (CT or MRI)	

CT Computed tomography; MRI Magnetic resonance imaging

When the diagnosis of Marfan syndrome has been established the diagnostic work-up should include at a minimum:

- A thorough clinical assessment
- ECG
- Chest x-ray
- Echocardiography Doppler evaluation especially for measurements of the ascending aorta and degree of mitral regurgitation
- MRI for measurements of the entire aorta and its branches and for lumbosacral dural ectasia, or abdominal ultrasound for the abdominal aorta; or computed tomography scanning for any of the above

A diagnostic workup may require:

- Coronary arteriography in patients over the age of 40 years (or younger if there are severe risk factors for coronary artery disease) in whom surgery is being planned
- TEE if aortic dissection is suspected

Part V – Indications for intervention

The following situations warrant surgical intervention:

- A maximal aortic root diameter greater than 55 mm
- A maximal aortic root greater than 50 mm in patients with a family history of dissection, rapid aortic root growth greater than 2 mm per year or severe aortic and/or mitral valve regurgitation that requires surgery
- Maximal aortic root diameter of greater than 45 to 50 mm if the surgeon believes that the aortic valve can be spared (a more aggressive view, especially if an aortic valve-sparing procedure is planned)
- A maximum aortic root dimension greater than 44 mm if pregnancy is desired
- Progressive dilation or a diameter of approximately 50 mm of other parts of the aorta
- Severe mitral regurgitation associated with symptoms or progressive left ventricular dilation and/or dysfunction

Grade: C
Level: IV
References: 96-100

Part VI – Surgical options

For aortic root replacement, the surgical options include the following: a composite graft repair (a modified Bentall procedure – using a mechanical, bioprosthetic or homograft aortic valve prosthesis) (96), or an aortic valve-sparing procedure (100). If necessary, all other parts of the aorta can be replaced. Surgery should be performed in a centre and by surgeons with substantial experience with these types of surgery.

Part VII – Surgical outcomes

The five and 10-year survival rates after aortic root replacement are 80% and 60%, respectively (98). This relatively poor outlook is mainly caused by the necessity for reoperation of the aorta because of the presence of preexisting type 1 dissection, or the development of new dilation or dissection of other parts of the aorta. A recent study reports a high survival rate at five years for selected Marfan patients who had aortic-valve sparing surgery (100). Longer term data are not yet available.

Part VIII – Arrhythmias

Arrhythmias are not a feature of Marfan syndrome itself. They may occur as a consequence of mitral regurgitation, myocardial ischemia and/or infarction due to dissection, or ventricular dysfunction.

Part IX – Pregnancy

For women with Marfan syndrome, pregnancy presents a two-fold problem. There is a genetic problem (because there is a 50% chance that the child will be affected), and there is an increased (but unquantified) risk of aortic dissection during pregnancy, and for up to six months postpartum.

Women with an aortic diameter above 44 mm should be strongly discouraged from becoming pregnant without repair of the arota. An aortic diameter below 40 mm rarely presents a problem, although a completely safe diameter does not exist.

Grade: C
Level: V
References: 101,102

Part X – Follow-up

Whenever possible, Marfan patients should be under the care of professionals with specific training and/or experience in Marfan syndrome. Ideally, this should be through a multidisciplinary clinic.

All patients with Marfan syndrome should be advised to take beta-adrenergic blocking agents, and to remain on them unless intolerable side effects preclude their use. This is especially true, usually in association with other blood pressure-lowering agents, if dissection has occurred.

During follow-up, the aortic root and the entire aorta should be regularly evaluated with echocardiography, MRI, computed tomography and/or abdominal ultrasound examinations. This is particularly true if a dissection remains and its stability is being monitored.

Patients with mitral valve prolapse and moderate to severe mitral regurgitation should also be followed up with yearly echocardiography.

Endocarditis prophylaxis is recommended for six months following aortic root replacement or for life if any residual gradient and/or lesions persist, or in the presence of prosthetic valve or mitral regurgitation.

Grade: Consensus
References: 100,102

APPENDIX I
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APPENDIX II
Levels of evidence used in developing the management recommendations for adults with congenital heart disease

Level of evidence	Grade of recommendation
Level I: Large randomized trials with clear-cut results and low risk of error	A
Level II: Randomized trials with uncertain results and/or moderate to high risk of error	B
Level III: Nonrandomized studies with contemporaneous controls	C
Level IV: Nonrandomized studies with historical controls	C
Level V: Case series without controls	C

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CCS Consensus Conference 2001 update: Recommendations for the Management of Adults with Congenital Heart Disease Part III

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The Congenital Heart Disease Committee of the American College of Cardiology, the Council on Cardiovascular Disease in the Young of the American Heart Association, the Grown-Up Congenital Heart Working Group of the European Society of Cardiology, the International Society for Adult Congenital Cardiac Disease and the Japanese Society for Adult Congenital Heart Disease have all endorsed this document. Canada is fortunate to have a nationwide group of national and regional adult congenital heart disease (ACHD) centres called the Canadian Adult Congenital Heart (CACH) Network (Appendix 1).

This material has been written in as user-friendly a fashion as possible. We envisaged a clinician looking up a lesion, and wishing to see the recommendations at a glance, rather than having to refer to other sections of the report. This has led to some repetition for the reader who begins at the beginning and ends at the end. *The repetitive portions are printed in italics to reduce frustrations resulting from this style.* We have given weight to our management recommendations. The scales that we used are shown in Appendix II. We have used standards similar to those used in past Canadian Cardiovascular Society (CCS) Consensus Conferences.

SECTION XI – COMPLETE TRANSPOSITION OF THE GREAT ARTERIES

Part I – Background information

Definition: There is atrioventricular concordance and ventriculoarterial discordance – ie, the right atrium connects to the morphological right ventricle, which gives rise to the aorta, and the left atrium connects to the morphological left ventricle, which gives rise to the pulmonary artery.

Approximately two-thirds of patients have no major associated abnormalities ('simple' transposition). Approximately one-third of patients have associated abnormalities ('complex' transposition). The most common associated abnormalities are ventricular septal defect (VSD) and pulmonary and/or subpulmonary stenosis.

Part II – History and management

Unoperated (simple) transposition is a lethal condition with 90% mortality in the first year of life. Thus, nearly all patients seen as adults will have had intervention.

The most common surgical procedure in patients who are adults is the atrial switch operation in the form of a

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Mustard or Senning procedure. Blood is redirected at the atrial level using a baffle (Mustard operation) or atrial flaps (Senning operation), achieving physiological correction, but the right ventricle continues to support the systemic circulation.

Now, the atrial switch operation has been supplanted by the arterial switch operation (Jatene), but few of these patients have yet become adults. Blood is redirected at the great artery level by switching the aorta and pulmonary arteries such that the left ventricle supports the systemic circulation. The coronary arteries are translocated to the neoaorta (formerly the pulmonary artery). The tissue loss in the sinuses of the neopulmonary artery is made good with a pericardial patch.

In a small proportion of patients (less than 10%) who have had a VSD and pulmonary and/or subpulmonary stenosis, a Rastelli operation will have been done. Blood is redirected at the ventricular level (with the left ventricular outflow tunnelled to the aorta), and a valved conduit is placed from the right ventricle to the aorta. The left ventricle supports the systemic circulation.

Rarely, in patients with a large VSD and established pulmonary vascular disease, a palliative atrial switch operation will have been done to improve oxygenation. This is an atrial switch operation but the VSD is left open (or enlarged). These patients resemble Eisenmenger VSDs and should be managed as such. (Section XV – Eisenmenger Syndrome).

Part III – Investigational recommendations in operated patients

Because most patients will have had an operation, investigations are directed toward postoperative sequelae and will vary according to the type of operation performed.

All patients should have at a minimum:

- *A thorough clinical assessment*
- *Electrocardiogram (ECG)*
- *Chest x-ray*
- Oximetry at rest and possibly with exercise

Patients who have had an atrial switch operation also require:

- *Echocardiography Doppler examination by an appropriately trained individual* to detect baffle obstruction, baffle leak or atrioventricular valve regurgitation, and to assess systemic ventricular function and subpulmonary obstruction
- A Holter monitor because of the high prevalence of sick sinus syndrome and atrial arrhythmias, and possible ventricular arrhythmias in older patients

and may require:

- Transesophageal echocardiogram (TEE) if there is inadequate visualization of the intra-atrial baffle on the transthoracic echocardiogram (TTE)
- Nuclear cardiology assessment of myocardial perfusion (if ischemia is suspected), or of ventricular function. Radionuclide angiography and magnetic resonance imaging (MRI) usually report better right ventricular function than does echocardiography
- MRI to evaluate baffle function (obstruction or leakage) and ventricular volumes, shapes and function
- Heart catheterization including coronary angiography if there are doubts about additional lesions and if surgical reintervention is planned, or if adequate assessment of the hemodynamics is not obtained by noninvasive means
- Exercise testing to evaluate functional capacity (including) heart rate and blood pressure response, and to assess whether arrhythmias may be provoked

Patients who have had an arterial switch operation also require:

- *Echocardiography Doppler examination by an appropriately trained individual* to assess right ventricular outflow tract obstruction (the most common problem), ventricular function, neoaortic root dilation, possible neoaortic valve regurgitation and coronary ostial status (although the last may be difficult to see in adults)
- Exercise stress testing periodically because of possible coronary ischemia due to reimplantation of the coronary arteries

and may require:

- Holter monitoring if arrhythmia is suspected. (The long term outcome following the arterial switch is unknown, but arrhythmias appear to be substantially less common than after the atrial switch operation)
- Nuclear cardiology assessment of myocardial perfusion periodically because coronary ischemia is possible due to reimplantation or redirection of the coronary arteries
- Coronary arteriography if ischemia is documented on noninvasive testing
- Complete heart catheterization if adequate assessment of the hemodynamics is not obtained by noninvasive means or additional lesions are suspected
- MRI to assess right ventricular outflow tract obstruction

Patients who have had a Rastelli operation also require:

- *Echocardiology Doppler examination by an appropriately trained individual* to assess right ventricle-to-pulmonary artery conduit stenosis and/or regurgitation, subaortic stenosis, aortic regurgitation, ventricular function and atrioventricular valve regurgitation. Assessment of the conduit gradient may be difficult, but it is usually possible to measure the right ventricular systolic pressure from the tricuspid regurgitation jet; this may be a useful surrogate in the absence of pulmonary hypertension

and may require:

- MRI to assess the issues above
- Heart catheterization to determine the severity of conduit stenosis or regurgitation, and the status of the distal pulmonary arteries if inadequate information is obtained from noninvasive testing and surgery is contemplated

Patients who have had a palliative atrial switch operation also require:

- *Echocardiography Doppler examination by an appropriately trained individual* to detect baffle obstruction, baffle leak or atrioventricular valve regurgitation, and to assess systemic ventricular function
- A Holter monitor because of the high prevalence of sick sinus syndrome and atrial arrhythmias
- Complete blood count, ferritin, clotting profile, renal function and uric acid (Section XVI – Management of Cyanotic Patients)

Part IV – Indications for reintervention

The following situations may warrant reintervention following the atrial switch procedure.

- Significant systemic (tricuspid) atrioventricular valve regurgitation
- Severe right or left ventricular dysfunction
- Symptomatic bradycardia, tachyarrhythmias or sick sinus syndrome
- Baffle leak resulting in a significant left-to-right shunt (greater than 1.5:1), any right-to-left shunt, symptoms or ventricular dysfunction
- Superior vena cava or inferior vena cava pathway obstruction
- Pulmonary venous obstruction (although this is usually seen early and will have been reoperated upon in childhood)

Grade: C
Level: V
References: 1-10

The following situations may warrant intervention following an arterial switch procedure.

- Significant right ventricular outflow tract obstruction at any level (pullback peak to peak gradient at catheterization greather than 50 mmHg or right ventricular/left ventricular pressure ratio greater than 0.6)
- Myocardial ischemia from coronary artery obstruction
- Neoaortic valve regurgitation
- Aortopulmonary collateral vessels

Grade: C
Level: V
References: 11-14

The following situations may warrant reintervention following the Rastelli procedure.

- Significant right ventricle-to-pulmonary artery conduit stenosis (pullback gradient at catheterization greater than 60 mmHg) or significant regurgitation
- Significant subaortic obstruction across the left ventricle-to-aorta tunnel
- Residual VSD
- Branch pulmonary artery stenosis

Grade: C
Level: V
References: 15,16

Part V – Surgical and/or interventional options

Patients who require reintervention should be treated by ACHD cardiologists and congenital heart surgeons with appropriate experience.

Grade: C
Level: V
References: 17,18

The following are possible intervention strategies.

- Surgery may be necessary for baffle stenosis or leakage in patients with an atrial switch procedure. Balloon dilation of the superior vena cava (SVC) or the inferior vena cava (IVC) stenosis is an option, but success is limited in adults. Pathway obstruction is less common after the Senning operation than after the Mustard operation, and is usually amenable to balloon dilation. SVC stenosis is usually benign, unlike IVC stenosis, which may be life-threatening. Stent insertion may be considered for SVC or IVC stenosis

- Patients with an atrial switch procedure and severe systemic (tricuspid) atrioventricular valve regurgitation may need valve replacement if systemic ventricular function is adequate, or possibly pulmonary artery banding to improve tricuspid regurgitation by altering septal geometry
- Patients with severe systemic (right) ventricular dysfunction and/or severe systemic (tricuspid) atrioventricular valve regurgitation following an atrial switch procedure may need to be considered for heart transplantation. A conversion procedure to an arterial switch following retraining of the left ventricle with a pulmonary artery band may be considered but this is experimental with little data available in adults (19-22)
- Patients who have had an arterial switch operation may require coronary artery bypass grafting (preferably with arterial conduits) for myocardial ischemia
- Patients who have had an arterial switch operation may require augmentation of the right ventricular outflow tract for outflow tract obstruction
- Patients who have had a Rastelli operation will need conduit replacement at some time
- Patients who have had a Rastelli operation may need left ventricle-to-aorta baffle revision because of obstruction
- Patients who have had a palliative atrial switch operation may require consideration of heart-lung transplantation
- The role of afterload reduction with angiotensin-converting enzyme (ACE) inhibitors or beta-blockers to preserve systemic right ventricular function is as yet unknown, but a major trial to address this question will soon be underway. Meanwhile, many patients are being treated empirically with ACE inhibitors

Part Vl – Surgical and/or interventional outcomes

The overall survival of patients who have had an atrial switch procedure is approximately 65% at 25 years of age, with increased likelihood of survival with later year of operation. Patients who have 'simple' transposition have a better survival (80% at 25 years of age) than those with 'complex' transposition (45% at 25 years of age). Causes of death include sudden unexpected (presumed arrhythmic) death, heart failure and baffle obstruction.

The long term survival data following the arterial switch are just beginning to emerge (19). Neoaortic root dilation, neoaortic valve regurgitation, right ventricular outflow tract obstruction and coronary artery stenosis and/or occlusion are recognized complications.

Following the Rastelli operation, repeated conduit changes will be necessary and there is a risk of deteriorating ventricular function. Sustained monomorphic ventricular tachycardia and supraventricular tachycardias may occur.

Patients who have had a palliative atrial switch probably have a prognosis similar to Eisenmenger VSD, but specific information is lacking. Quality of life is generally improved for a time, however.

Part VII – Arrhythmia

Atrial flutter (intra-atrial re-entry) occurs in 20% of atrial switch patients by age 20 years of age, and progressive sinus node dysfunction and/or junctional rhythm is seen in half of the patients by that time (4,8,9,23,24).

Transvenous pacemaker insertion for symptomatic bradycardia or antitachycardia pacing for some atrial arrhythmias may be required. In patients with an atrial switch operation, transvenous pacing leads must traverse the upper limb of the atrial switch to enter the morphological left atrium and/or left ventricle. Active fixation is required.

Transvenous pacing for bradyarrhythmias following intra-atrial repair for transposition can be performed when needed (15% to 20% of adult patients) by experts. Baffle leak must be ruled out by TEE before transvenous pacemaker insertion to reduce the risk of paradoxical embolism, and morphological assessment of the systemic venous pathway should be performed to rule out a stenotic systemic channel. Epicardial leads are a good alternative when venous access is troublesome.

Grade: C
Level: V
References: 25

Transcatheter ablation procedures for intra-atrial re-entry tachycardia and/or atrial flutter and atrioventricular nodal re-entry is feasible, with an initial rate of success in these patients of 60% to 70% (26). Ablation in these patients is more complex and associated with a lower cure rate because of both the complex anatomy and the previous surgical scars; ablation should be undertaken by an electrophysiologist with appropriate training and/or experience in this population.

Part VIII – Pregnancy

Pregnancy in women with a normal functional class following atrial switch operation is usually well tolerated. Worsening of systemic right ventricular function during or shortly after pregnancy, however, is reported in about 10% of patients (27,28). ACE inhibitors should be stopped before pregnancy occurs.

Part IX – Follow-up

All patients should have regular cardiology follow-up by an ACHD cardiologist. Endocarditis prophylaxis is recommended.

Grade: Consensus

SECTION XII – CONGENITALLY CORRECTED TRANSPOSITION OF THE GREAT ARTERIES

Part I – Background information

Transposition of the great arteries (TGA) involves atrioventricular discordance and ventriculoarterial discordance (double discordance). Systemic venous return to the right atrium enters the morphological left ventricle, which ejects blood into the pulmonary artery. Pulmonary venous return is to the left atrium and then by the morphological right ventricle to the aorta. The circulation is physiologically corrected, but the systemic circulation is supported by the morphological right ventricle (hence the term 'ventricular inversion' that has been used for this condition).

Congenitally corrected transposition may exist in the setting of univentricular heart, but this is not considered further here.

It is rare (less than 1% of congenital heart defects) but accounts for a high percentage of cyanotic patients undergoing surgery as adults. Associated anomalies occur in up to 98% in some series and consist of VSD (75% of cases), pulmonary or subpulmonary stenosis (75% of cases), and systemic (tricuspid) valve anomalies (Ebstein-like in 30% of cases). Congenital complete heart block occurs in 5% of cases.

Part II – Prevalence and genetics

A large survey did not show an elevated rate of cardiac malformations in parents (0.6%) or siblings (0.8%) of patients with different forms of TGA (29). Although single case reports of chromosome 22q11 deletion in cases of TGA exist, a large study did not confirm this association (30).

Part III – History and management of unoperated patients

Patients with no associated abnormalities may survive until the sixth or seventh decade, and may go unrecognized until problems arise. Progressive systemic (tricuspid) atrioventricular valve regurgitation and systemic (right) ventricular dysfunction, which may present as acute pulmonary edema, tend to occur from the fourth decade onwards. The presence of significant systemic tricuspid atrioventricular regurgitation negatively affects the survival of this patient population (31). Atrial arrhythmias are common from the fifth decade onwards. In addition to congenital complete atrioventricular block, acquired complete atrioventricular block continues to develop at a rate of 2% per year (32), and is especially common at the time of heart surgery. Pulmonary (mitral) atrioventricular valve regurgitation may occasionally occur, and subpulmonary (morphological left) ventricular dysfunction or outflow tract obstruction may also develop and progress.

The outcome of patients with pulmonary stenosis and/or VSD who have a balanced pulmonary circulation (without excessive pulmonary blood flow on the one hand or excessive pulmonary stenosis on the other hand) is similar with or without operation.

Part lV – Diagnostic work-up

An adequate diagnostic work-up:

- Documents the anatomy described above
- Identifies and quantifies associated abnormalities that may influence management (VSD, pulmonary and/or subpulmonary stenosis, systemic [tricuspid] atrioventricular valve regurgitation, ventricular function and atrioventricular block)

The diagnostic workup should include at a minimum:

- *A thorough clinical assessment*
- *ECG*
- *Chest x-ray*
- *Echocardiography Doppler examination by an appropriately trained individual*
- Exercise or cardiopulmonary testing with oximetry

The diagnostic workup may require:

- TEE examination to assess ventricular function, atrioventricular valve regurgitation and pulmonary outflow tract if this information is not provided by a TTE study, particularly in the operated patient. These patients are often very difficult to image on TTE because of a poor echocardiography window
- A complete heart catheterization to assess the hemodynamics, especially in the operated patient who has a conduit between the left ventricle and pulmonary artery, or the unoperated patient who is being considered for surgery
- *Coronary angiography in patients at risk of coronary artery disease or if the patient is over the age of 40 years and surgery is planned*
- Holter monitor for atrioventricular block and atrial arrhythmia assessment
- Nuclear cardiology assessment of ventricular function. Radionuclide angiography and MRI usually report better right ventricular function than does echocardiography
- MRI to evaluate ventricular volumes, ventricular function or conduit function
- Complete blood count, ferritin, clotting profile, renal function and uric acid if the patient is cyanosed (Section XVI – Management of Cyanotic Patients)

Part V – Indications for intervention

Patients with a VSD and pulmonary outflow tract obstruction are frequently cyanotic and may have been palliated with systemic-to-pulmonary artery shunts in childhood. Significant cyanosis (oxygen saturation less than 90%) in the absence of severe pulmonary hypertension should be an indication for intracardiac repair.

The following situations may warrant intervention.

- The presence of VSD
- Pulmonary or subpulmonary stenosis (pullback gradient at catheterization greater than 60 mmHg)
- The presence of moderate or greater systemic (tricuspid) atrioventricular valve regurgitation
- Complete atrioventricular block that requires pacemaker implantation for symptoms, progressive or profound bradycardia or poor exercise heart rate response
- Symptomatic deterioration

Grade: C
Level: V
References: 15,32-37

The following situations may warrant reintervention.

- Residual VSD
- Stenosis across a prior left ventricle-to-pulmonary artery conduit (pullback gradient at catheterization greater than 60 mmHg)
- Moderate or worse systemic (tricuspid) atrioventricular valve regurgitation following prior surgical repair
- Deteriorating systemic (right) ventricular function
- Failing pacemaker
- Important pulmonary and/or subpulmonary stenosis

Grade: C
Level: V
References: 38-40

Part VI – Interventional options

Patients who require intervention or reintervention should be treated by ACHD cardiologists and congenital heart surgeons with appropriate experience.

Grade: C
Level: V
References: 17,18

Occasionally, patients may be unsuitable for repair because of small pulmonary arteries, small systemic (right) ventricles or straddling atrioventricular valves, and may require palliative shunt procedures.

VSD closure alone is almost always performed in childhood with the VSD patch placed to avoid atrioventricular block.

Balloon dilation of pulmonary stenosis may lead to complete atrioventricular block and is not recommended.

Repair may involve implantation of a valved conduit from the pulmonary (left) ventricle to the pulmonary artery and repair of the VSD(s). Alternatively, the Ilbawi approach involves tunnelling the left ventricle to the aorta, a right ventricle-to-pulmonary artery conduit and an atrial switch (Mustard procedure). Thus, the morphological left ventricle and mitral valve support the systemic circulation. Adult data are lacking regarding the use of the Ilbawi approach (in the setting of VSD and pulmonary stenosis) or a double switch (ie, Mustard operation and an arterial switch if there is no pulmonary stenosis). Such procedures should still be considered experimental in adult patients.

Patients with systemic (tricuspid) regurgitation presenting for surgery will usually require valve replacement. Repair is usually impractical because the valve is usually morphologically abnormal. Surgery should be performed before systemic ventricular function deteriorates. The Ilbawi approach, leaving the regurgitant tricuspid valve on the pulmonary side may be an option but is still experimental in the adult.

Grade: C
Level: V
References: 33,37

Patients with deteriorating systemic (right) ventricular function (which commonly appears after surgical repair) should be treated aggressively with medical therapy but may need to be considered for transplantation. Deterioration may be rapid. The role of ACE inhibitors in preserving systemic right ventricular function is as yet unknown, but many patients are treated empirically with afterload reduction while clinical trial data are awaited.

Complete atrioventricular block is not uncommon after surgery and necessitates pacing.

In isolated pulmonary and/or subpulmonary stenosis, direct enlargement of the outflow tract and valve is seldom possible because of the wedging of the outflow tract and the close relation to the conducting system and left coronary artery, and a pulmonary (left) ventricle-to-pulmonary artery conduit is often required.

Part VII – Interventional outcomes

Of patients with congenitally corrected transposition operated or unoperated who reach adulthood, median survival is 40 years. Survival is better if there are no associated anomalies, but the overall survival of these patients is still very poor compared with that of the general population (41). Usual causes of death are sudden (presumed arrhythmic) and progressive ventricular dysfunction with systemic (tricuspid) atrioventricular valve regurgitation.

Following surgical repair of VSD and/or subpulmonary stenosis, rapidly progressive systemic (tricuspid) atrioventricular valve regurgitation is well recognized. Medical therapy is often tried, but valve replacement is usually required.

Part VIII – Arrhythmias

Atrial fibrillation is common in operated patients and may be related to systemic (tricuspid) atrioventricular valve regurgitation.

If atrial fibrillation occurs, both anticoagulants and antiarrhythmic therapy are usually required. Backup pacing may also be necessary. Reparative surgery at the tricuspid valve level does not seem to prevent recurrence of atrial arrhythmias (42).

Complete atrioventricular block requires the insertion of a permanent pacemaker. The optimal modality is DDD but is not always possible. Active fixation electrodes are required.

Transvenous pacing should be avoided if there are intracardiac shunts because paradoxical emboli may occur. Epicardial leads are preferred under these circumstances. For the same reason, venous thromboemboli from any source are a potential hazard. Anticoagulants should be used if a source of venous thromboembolism is found.

Grade: C
Level: V
References: 25

Part IX – Pregnancy

Pregnancy may be associated with a marked deterioration in systemic right ventricular function and/or the development or worsening of systemic (tricuspid) atrioventricular valve regurgitation. In two series of 19 and 22 patients with congenitally corrected TGA, a total of 105 pregnancies were reported (43,44). There were no maternal deaths, but substantial maternal morbidity and fetal losses were observed. Close supervision of pregnant patients is recommended.

Part X – Follow-up

All patients should have regular cardiology follow-up by an ACHD cardiologist.

Particular attention should be paid to:

- Ventricular function (deteriorating systemic ventricular function may require consideration of afterload reduction and/or transplantation)
- Systemic (tricuspid) atrioventricular valve regurgitation
- Complete atrioventricular block
- Atrial fibrillation

Endocarditis prophylaxis is recommended.

Grade: Consensus

SECTION XIII – FONTAN OPERATION

Part I – Background information

Definition: The Fontan operation is a palliative procedure for patients with a functionally or anatomically single ventricle or complex malformation considered unsuitable for biventricular repair. There is diversion of all of the systemic venous return to the pulmonary arteries, usually without employing a subpulmonary ventricle.

Originally described for patients with tricuspid atresia, it has now been extended to most forms of single ventricle circulation.

There are numerous variations in the surgical approach. The most likely types of Fontan procedure to be encountered are: the direct right atrium to pulmonary artery connection; the total cavopulmonary connection (SVC to pulmonary artery and IVC to pulmonary artery through an intra-atrial tunnel); the extracardiac conduit (SVC to pulmonary artery and IVC to pulmonary artery through an external conduit); and right atrium to right ventricle through a valved conduit when right ventricular size and function are adequate. The Fontan procedure may be performed as a single or staged procedure (with a classic or bidirectional Glenn shunt performed as the first procedure, followed by the completion of the Fontan as a second procedure).

Part II – History and management of operated patients

Patients who have had a Fontan operation are at risk from the following.

- Arrhythmias: Atrial flutter and/or fibrillation is common and increases with increasing duration of follow-up. This can be associated with profound hemodynamic deterioration and needs prompt medical attention. Heart block may also occur late and is often associated with hemodynamic deterioration (45).

When arrhythmias are present, an underlying hemodynamic cause should always be sought, and in particular, obstruction of the Fontan circuit needs to be excluded.

Grade: C
Level: V
References: 46

- Thromboembolism (both systemic and pulmonary) may be associated with atrial fibrillation; may be related to a sluggish circulation, especially in the systemic veins and right atrium; and may be related to clotting abnormalities (eg, protein C deficiency) (47).

- Protein-losing enteropathy (PLE) occurs in up to 10% of postoperative Fontan patients, and is associated with ascites, peripheral edema, pleural and pericardial effusions, chronic diarrhea and elevated stool alpha$_1$ antitrypsin levels (48)
- Progressive deterioration of ventricular function with or without atrioventricular valve regurgitation may be part of the natural history of a patient with a single ventricle
- Hepatic dysfunction is usually due to hepatic congestion
- Right pulmonary vein compression and/or obstruction is due to compression from the enlarged right atrium or atrial baffle bulging into the left atrium
- Cyanosis: Worsening cyanosis may relate to worsening of ventricular function, the development of venous collateral channels draining to the left atrium or the development of pulmonary arteriovenous malformation (especially if a classic Glenn procedure remains as part of the Fontan operation)

Part III – Investigational recommendations

Particular attention should be paid to:

- Ventricular function, both systolic and diastolic
- Systemic atrioventricular valve regurgitation
- Obstruction at the Fontan anastomosis
- Residual shunts
- The detection of thrombus within the right atrium
- Increasing cyanosis
- The development of atrial flutter or fibrillation
- The detection of pulmonary arteriovenous malformations resulting in increased cyanosis (especially when a classic Glenn procedure remains)
- Serum protein and albumin levels
- Hepatic function

Investigations are directed toward postoperative sequelae and will vary according to the type of operation performed.

All patients should have at a minimum:

- *A thorough clinical assessment*
- *Oximetry at rest*
- *ECG*
- *Chest x-ray*
- *Echocardiography Doppler examination by an appropriately trained individual* to assess systemic ventricular function, atrioventricular valve regurgitation, the presence or absence of residual shunts, the presence or absence of obstruction in the Fontan circuit and of spontaneous contrast ('smoke') in the atrium
- Serum protein and albumin measurement. If low, increased alpha$_1$ antitrypsin clearance in the stool documents the presence of PLE

The diagnostic workup may require:

- Echocardiography with a bubble study to rule out pulmonary arteriovenous malformations
- TEE if there is inadequate visualization of the Fontan anastomosis or to exclude thrombus in the atrium
- MRI if the Fontan anastomosis cannot be assessed reliably by TEE or to assess ventricular function
- Nuclear angiography to evaluate ventricular function
- Complete heart catheterization if surgical reintervention is planned or if adequate assessment of the hemodynamics is not obtained by noninvasive means. Even small gradients between the atrium and pulmonary artery (or outflow chamber) may suggest important obstruction across the Fontan anastomosis

Part IV – Indications for reintervention

The following situations may warrant reintervention.

- Residual atrial septal defect (ASD) resulting in a significant right-to-left shunt, symptoms or cyanosis
- Residual shunt secondary to a previous palliative surgical shunt or residual ventricle-to-pulmonary artery connection
- Significant systemic atrioventricular valve regurgitation
- Obstruction in the Fontan circuit
- Development of venous collateral channels or pulmonary arteriovenous malformations
- Development of sustained atrial flutter or fibrillation (an immediate attempt to restore sinus rhythm is crucial once right atrial thrombus has been excluded)
- Development of PLE
- Pulmonary venous obstruction
- High degree atrioventricular block or sick sinus syndrome necessitating pacemaker insertion
- Planned closure of a fenestrated Fontan (transcatheter)

Grade: C
Level: V
References: 49-52

Part V – Surgical/interventional options

Patients who require reintervention should be treated by ACHD cardiologists and congenital heart surgeons who have appropriate training and/or experience.

Grade: C
Level: V
References: 17,18

The following are possible intervention strategies.

- Patients with systemic atrioventricular valve regurgitation may require atrioventricular valve repair or replacement
- Patients with residual shunts of significance may require closure of the residual shunt
- Patients with significant obstruction at the Fontan anastomosis may be candidates for balloon angioplasty, stenting or surgical revision of the Fontan connection
- Patients whose anastomosis is a valved conduit (right atrium to right ventricle connection) may need Fontan revision or conversion to a different form of Fontan
- Patients with venous collateral channels or arteriovenous malformation may need transcatheter occlusion or conversion of a classic Glenn shunt to a bidirectional Glenn, respectively
- Patients with poorly controlled atrial flutter may be candidates for catheter ablation
- Conversion of a classical Fontan to a lateral tunnel or external conduit with concomitant atrial maze procedure may be considered for the treatment of serious refractory atrial arrhythmias
- If permanent pacing is required, epicardial atrioventricular sequential pacing should be employed whenever possible to reduce the risk of thromboembolism
- Patients with PLE may be candidates for the creation of a fenestration in the atrial septum or revision of the Fontan. Alternatively, subcutaneous heparin, octreotide treatment and prednisone therapy have also been tried with variable success. No therapy seems more successful than the others
- Transplantation may be necessary for systemic ventricular failure or intractable PLE

The role of long term anticoagulation is contentious. It is recommended that patients with a history of documented atrial flutter or fibrillation, fenestration in the Fontan connection or spontaneous contrast ('smoke') in the right atrium on echocardiography be anticoagulated.

Grade: Consensus
References: 53,54

Part VI – Surgical and/or interventional outcomes

The Fontan operation remains a palliative, not a curative, procedure.

The reported average 10-year survival following Fontan operation is approximately 60%, rising to 80% under ideal circumstances (55,56).

If PLE develops, the five-year survival is approximately 50%. Reoperation following the Fontan procedure carries a high mortality, and with PLE the mortality may be as high as 75%. If obstruction in the Fontan circuit is the cause of the PLE, however, successful revision of the Fontan anastomosis may cure the PLE.

Usual causes of death are those related to ventricular failure, arrhythmias, reoperation and PLE.

Part VII – Arrhythmias

Atrial flutter and/or fibrillation is common (15% to 20% at five-year follow up), and increases with duration of follow-up. It carries significant morbidity, can be associated with profound hemodynamic deterioration and needs prompt medical attention. Patients at greater risk for atrial tachyarrhythmias are those who were operated on at an older age with an atriopulmonary connection, who have poor ventricular function, systemic atrioventricular valve regurgitation or increased pulmonary artery pressure. When atrial flutter and/or fibrillation is present, an underlying hemodynamic cause should always be sought, and in particular, evidence for obstruction of the Fontan circuit needs to be sought. Patients not anticoagulated, presenting with atrial flutter and/or fibrillation should have intravenous heparin started immediately and transesophageal echocardiography performed to rule out the presence of thrombus. Prompt attempts should be made to restore sinus rhythm if no thrombus is found and/or if there is hemodynamic compromise. Antiarrhythmic medications, alone or combined with an antitachycardia pacing device, and radiofrequency catheter ablation techniques, have had limited success. Surgical conversion from an atriopulmonary Fontan to a total cavopulmonary connection with concomitant atrial cryoablation (for flutter) therapy and maze procedure (for fibrillation) at the time of surgery has been reported with good short term success (57). Patients with atrial arrhythmias (including paroxysmal) should be anticoagulated with warfarin long term.

Sinus node dysfunction and complete heart block can occur and require pacemaker insertion. Endovenous ventricular pacing through the coronary sinus is possible, but epicar-

dial atrioventricular sequential pacing should be employed whenever possible to reduce the risk of thromboembolism.

Part VIII – Pregnancy

Pregnancy carries additional risks to the mother because of the increased hemodynamic burden on the single ventricle and atrium (58,59). There is an increased risk of:

- Systemic venous congestion
- Deterioration in ventricular function
- Worsened systemic atrioventricular valve regurgitation
- Atrial arrhythmias
- Thromboemboli
- Paradoxical emboli if the Fontan is fenestrated

Pregnancy is possible, however, with very careful patient selection, and meticulous cardiac and obstetric supervision (58).

Part IX – Follow-up

All patients who have had a Fontan operation should be followed up yearly by an ACHD cardiologist.

Endocarditis prophylaxis is often recommended.

Grade: Consensus

SECTION XIV – SINGLE VENTRICLE

Part I – Background information

Anatomy: Patients with single ventricles either have an 'anatomically' single ventricle made up of a single pouch of indeterminate origin or, more commonly, have a 'functionally' single ventricle with one well-formed ventricle accompanied by a second underdeveloped or rudimentary ventricle. The atrium can be situs solitus, inversus or ambiguous. The atrioventricular valves guarding the inlet of the univentricular heart can consist of two separate valves (double inlet left ventricle, double inlet right ventricle [DIRV]), one patent valve and one atretic valve (tricuspid atresia, mitral atresia), or a common valve (unbalanced atrioventricular septal defect). The well developed ventricular chamber can be of the left ventricular type with an anterosuperior right ventricular pouch or, less commonly, of a right ventricular type with a posterior left ventricular pouch (DIRV). The ventriculoarterial connection can be concordant or discordant, or the great arteries can arise from the same ventricle and be patent or stenotic (60,61).

Part II – History and management of unoperated patients

Patients with an 'ideal' anatomy (ie, a functionally single morphological left ventricle) with a 'well balanced' circulation (ie, some degree of pulmonic stenosis to avoid excessive pulmonary blood flow) may achieve late survival with good ventricular function, exercise capacity and minimal symptoms (62). The prognosis of all patients with unoperated univentricular hearts, however, is poor with a median survival of 14 years of age (death rate of 4.8% per year) with the majority being symptomatic with cyanosis and exercise intolerance (63).

Part III – Diagnostic workup

An initial diagnostic work-up should:

- Assess the anatomy and document the situs of the atria, status of the inlet atrioventricular valves (number, patency, and presence or absence of straddling), and morphology of the main ventricular chamber, as well as the position and patency of the great arteries
- Document the etiology of cyanosis (decreased pulmonary blood flow, arteriovenous mixing or pulmonary hypertension) and assess pulmonary resistance
- Identify other factors affecting the clinical condition of the patient (see complications and clinical sequelae of cyanotic heart disease)

The diagnostic work-up should include at a minimum:

- *A thorough clinical assessment*
- *ECG*
- *Chest x-ray*
- *Echocardiographic Doppler evaluation by an appropriately trained individual*
- Oximetry at rest and perhaps with exertion (if the saturation at rest is more than 90%)
- Complete blood count, ferritin, clotting profile, renal function and uric acid (Section XVI – Management of Cyanotic Patients)

The diagnostic work-up may require:

- TEE to visualize the anatomy in terms of atrial situs, atrioventricular connections, ventricular type and great arteries connections, as well as patency. (Caution should be exercised with sedation)
- MRI to visualize the anatomy, assess ventricular sizes and function, and evaluate associated lesions
- Nuclear angiography to quantify ventricular function
- Cardiopulmonary testing to evaluate functional capacity objectively, the degree and basis for exertional limitation, and exercise desaturation
- Heart catheterization to determine pulmonary artery pressures and resistances if these have not been adequately defined by other investigations

Part IV – Indications for intervention

Significant functional limitation, resting saturation less than 90%, dilated (volume overloaded) systemic ventricle and paradoxical embolism are indications for intervention.

Part V – Interventional options

Aortopulmonary shunt: The aortopulmonary shunt is rarely performed as the sole intervention any more.

Bidirectional Glenn: The bidirectional Glenn is usually performed in infancy as a staged procedure before the Fontan procedure (one ventricle repair), or performed as a 'definitive palliation' when patients are too high risk for Fontan surgery. It provides a controlled source of pulmonary blood flow while volume unloading the systemic ventricle (64).

Bidirectional Glenn plus additional pulmonary blood flow. An additional source of pulmonary blood flow by the pulmonary artery through a pulmonary artery band or native pulmonary stenosis, or through a Blalock-Taussig shunt, is sometimes added in conjunction with a bidirectional Glenn procedure to increase oxygen saturation at the expense of an increased volume load on the systemic ventricle (65).

One ventricle repair: Especially when the rudimentary pulmonary ventricle is less than 30% of its normal volume, the Fontan procedure allows systemic venous return to enter directly into the pulmonary circulation, bypassing the pulmonic ventricle or outlet chamber (Section XIII – Fontan Operation).

One and one-half ventricle repair. Sometimes when the rudimentary pulmonic ventricle is between 30% and 80% of its normal volume, the IVC blood flow is permitted to return to the pulmonary circulation by the pulmonic ventricle, whereas the SVC blood returns directly to the pulmonary circulation by a bidirectional Glenn procedure (66).

Two ventricles repair: In some instances, when the pulmonic ventricle is greater than 80% of its normal volume, a biventricular repair or ventricular septation may be feasible. Straddling of the atrioventricular valves and TGA may complicate this type of repair.

Transplantation: Heart transplantation for ventricular failure or heart and lung transplantation for ventricular failure with pulmonary hypertension should be considered when the patient is symptomatic and further palliation and/or repair is not possible.

Part VI – Interventional outcomes

Aortopulmonary shunt: Of the patients who survived to adulthood, there is at best a 50% survival at 20 years' follow-up (67,68). Systemic ventricular dilation and failure, as well as the development of arrhythmias (mainly atrial fibrillation and/or flutter), occur commonly.

Bidirectional Glenn: There is a 50% survival at 20 years follow-up (68,69). Progressive cyanosis may be due to a greater contribution of IVC blood flow compared with SVC blood flow with somatic growth (as seen in childhood) or, as is typical in adults, from the development of pulmonary arteriovenous fistulae.

Bidirectional Glenn plus additional pulmonary blood flow: No long term studies are available. By increasing volume loading on the systemic ventricle, the additional pulmonary blood flow may confer an actual survival disadvantage in these patients (63).

One ventricle repair. There is an 81% survival at 10 years for 'the perfect' Fontan candidate (55) compared with 60% survival at 10 years for all Fontan patients (56). Complications after a Fontan procedure include atrial arrhythmias, thrombus formation, PLE (especially if the Fontan procedure was performed in adults [70]), as well as systemic ventricular failure and progressive atrioventricular valve regurgitation (see Fontan section XIII).

One and one-half ventricle repair. No long term studies are available. The main long term complication of a bidirectional Glenn procedure, namely progressive formation of pulmonary atrioventricular fistulae, has not been documented at four years follow-up following a one and one-half ventricular repair (71).

Two ventricle repair. A complex biventricular repair (needing valved conduit or complex intraventricular tunnel) may not be preferable in the short or intermediate term to a simple one or one and one-half ventricular repair (72).

Transplantation. The outcome of heart transplantation in adult patients with congenital heart disease approaches that of adult patients without congenital heart problems with a one-year survival of 79% and a five-year survival of 60% (73). The outcome of heart and lung transplantation is less with a one-year survival of 60% to 80%, and a 10-year survival of 30% (74,75).

Part VII – Arrhythmias

Shunt. Patients palliated with an aortopulmonary shunt will develop significantly more atrial fibrillation or flutter at 30 years follow-up than patients palliated with a cavopulmonary shunt (35% versus 15%). Progressive systemic ventricular dysfunction has been linked to the development of atrial arrhythmias (68).

One ventricle repair. Section XIII – Fontan Operation.

Part VIII – Pregnancy

Shunt: Pregnancy is often well tolerated in a single ventricle patient with good functional class, good ventricular function and an oxygen saturation greater than 85% (Section XVI – Management of Cyanotic Patients). The risk of paradoxical emboli in these patients is high, and meticulous attention should be paid to avoid deep venous thrombosis in these patients.

One ventricle repair. Section XIII – Fontan Operation.

Part IX – Follow-up

Yearly follow-up by an ACHD cardiologist is recommended. Yearly clinical visit to follow functional status and oxygen saturation, as well as a yearly echocardiography to assess systemic ventricular function, semilunar valve stenosis and atrioventricular valve regurgitation should be performed. Complete blood count, ferritin, clotting profile, renal function and uric acid should be obtained on a yearly basis as well (Section XVI – Management of Cyanotic Patients).

Endocarditis prophylaxis is recommended.

SECTION XV – EISENMENGER SYNDROME

Part I – Background information

Eisenmenger syndrome, a term first used by Paul Wood (76), is defined as pulmonary vascular obstructive disease that develops as a consequence of a large pre-existing left-to-right shunt such that pulmonary artery pressures approach systemic levels and the direction of the flow becomes bidirectional or right-to-left. Congenital heart defects that can lead to the Eisenmenger syndrome include 'simple' defects such as ASD, VSD and patent ductus arteriosus (PDA) as well as more 'complex' defects such as atrioventricular septal defect, truncus arteriosus, aortopulmonary window, complex pulmonary atresia and univentricular heart. The high pulmonary vascular resistance is usually established in infancy (by age two years, except in ASD), and can sometimes be present from birth.

Part II – History and management of unoperated patients

Patients with defects that allow free communication between the pulmonary and systemic circuits at the aortic or ventricular levels usually have a fairly healthy childhood (if no early congestive heart failure), and gradually become progressively cyanotic with each succeeding decade. Exercise intolerance (dyspnea and fatigue) is proportional to the degree of hypoxemia or cyanosis. In the absence of complications, these patients generally have a good functional capacity up to their third decade (77,78), and thereafter usually experience a slowly progressive decline in their physical abilities.

In patients with medium or large ASDs, Eisenmenger physiology usually appears later, often associated with pregnancy, recurrent thromboembolism or the development of primary or other secondary causes of pulmonary hypertension. Such additional factors may be required in ASD patients to develop this physiology, although this is a contentious point.

Complications from Eisenmenger syndrome tend to occur from the third decade onward. Congestive heart failure, the most serious complication, usually occurs after age 40 years (77).

Other complications include:

- Angina pectoris
- Arrhythmias (atrial fibrillation and/or flutter)
- Bleeding disorders
- Brain abscess
- Erythrocytosis
- Hemoptysis
- Hyperuricemia and/or gout
- Infective endocarditis
- Paradoxical emboli
- Pulmonary arterial aneurysm and/or calcification
- Progressive valvar stenosis and/or regurgitation
- Renal dysfunction (especially proteinuria)
- Sudden death
- Stroke and/or transient ischemic attack

Most patients with Eisenmenger syndome survive to adulthood (78-80) with a reported 77% and 42% survival rate at 15 and 25 years of age, respectively (78).

The most common modes of death associated with Eisenmenger syndrome are sudden death (30%), congestive heart failure (25%) and hemoptysis (15%). Pregnancy, perioperative mortality following noncardiac surgery and infectious causes (brain abscesses and endocarditis) account for most of the remainder of these deaths (77,78,80).

Part III – Diagnostic work-up

An adequate diagnostic work-up:

- Documents the presence of one or more communications between the systemic and pulmonary circuits at the great vessel, ventricular or atrial level
- Documents the existence of severe pulmonary hypertension with significant right-to-left shunting (saturation less than 90%)
- Identifies other factors affecting the clinical condition of the patient (see complications and clinical sequelae)

The diagnostic work-up should include at a minimum:

- *A thorough clinical assessment* including examination of the toes looking for differential cyanosis
- *ECG*
- *Chest x-ray*
- *Echocardiography Doppler evaluation by an appropriately trained individual*
- Oximetry at rest, and occasionally with exertion (if the saturation at rest is more than 90%)
- Blood work (complete blood count, ferritin, clotting profile, creatinine, uric acid) (Section XVI – Management of Cyanotic Patients)

The diagnostic work-up may require:

- MRI to visualize the defect(s) between the pulmonary and systemic circuits or to define better its/their location(s) and size(s), to evaluate the size of the proximal pulmonary arteries and to determine the presence of mural or obstructive thrombi
- TEE (rarely) to visualize defects between the pulmonary and systemic circuits or to define better its/their location(s) and size(s). Caution should be exercised with sedation because of the risk of systemic hypotension with consequent increase in right to left shunting
- Spiral/high resolution computed tomography (CT) scan of the chest in patients with hemoptysis to rule out the possibility of major pulmonary hemorrhage, especially in the setting of a chest x-ray showing pulmonary infiltrate
- Heart catheterization with pulmonary vasodilators primarily to determine pulmonary artery pressures and resistances if these have not been adequately defined by other investigations, and to rule out potentially reversible pulmonary vascular disease

- Open lung biopsy only when the reversibility of the pulmonary hypertension is uncertain from the hemodynamic data. It is potentially hazardous and should only be performed at centres that have substantial relevant experience in congenital heart disease

Part IV – Indications for intervention

The current underlying management principle in patients with Eisenmenger syndrome is to avoid any factors that may destabilize the delicately balanced physiology. In general, an approach of nonintervention is recommended.

The main interventions, therefore, are directed toward preventing complications (eg, influenza shots to reduce the morbidity of respiratory infections) or to restore the physiological balance (eg, iron replacement for iron deficiency, antiarrhythmic management of atrial arrhythmias, salt restriction and diuretics for right-sided heart failure, etc).

Hyperviscosity symptoms, in the absence of volume depletion, should be treated with isovolumic phlebotomy unless iron deficiency is present, in which case iron supplementation (and not phlebotomy) becomes the treatment of choice (Section XVI – Management of Cyanotic Patients).

Hypovolemia should be avoided. Any cause of hypovolemia may lead to hypotension and hypoxemia. Volume expansion should be provided immediately.

Noncardiac surgery should be performed only when necessary because of its high associated mortality (77,81). An experienced cardiac anesthetist with an understanding of Eisenmenger physiology should administer anesthesia. Eisenmenger patients are particularly vulnerable to alterations in hemodynamics induced by anesthesia or surgery, such as a minor decrease in systemic vascular resistance that can increase right-to-left shunting and possibly potentiate cardiovascular collapse. Local anesthesia should be used whenever possible. Avoidance of prolonged fasting and especially dehydration, the use of antibiotic prophylaxis when appropriate (82) and careful intraoperative monitoring (sometimes with an arterial line with or without a central venous line to allow early detection of sudden pressure and volume changes during surgery) are recommended (81,83). The choice of general versus epidural-spinal anesthesia is controversial. An experienced cardiac anesthetist with an understanding of Eisenmenger physiology should administer anesthesia. Additional risks of surgery are excessive bleeding, postoperative arrhythmias and deep venous thrombosis with paradoxic emboli. An 'air filter' or 'bubble trap' should be used for any intravenous lines. Early ambulation is recommended (81,83). Postoperative care in an intensive care unit setting is optimal (84,85).

As a general rule, hemoptysis should lead to a chest x-ray, a complete blood count, a clinical decision as to whether the patient needs hospital admission and often CT scanning to look for pulmonary hemorrhage or secondary cause. Bed rest should be implemented and, while usually self-limiting, each such episode should be regarded as potentially life-threatening. A treatable cause should be excluded, although it is most commonly due to bleeding bronchial vessels or pulmonary infarction.

Transplantation: Young age at presentation, recent worsening in functional class, history of syncope, right-sided failure and supraventricular arrhythmias are harbingers of poor prognosis and should accelerate the decision-making process regarding timing of transplantation (77,78,86).

The following carry increased risk in patients with Eisenmenger syndrome.

- Pregnancy (contraindicated)
- General anesthesia
- Dehydration
- Hemorrhage
- Noncardiac surgery
- Cardiac surgery
- Certain drugs eg, vasodilators, diuretics, some oral contraceptive pills, danazol, nonsteroidal anti-inflammatory drugs
- Anemia most commonly due to iron deficiency
- Cardiac catheterization
- Intravenous lines (because of the risk of paradoxical air embolism and infection)
- Altitude exposure
- Pulmonary infections

Grade: C
Level: V
References: 85,87,88,89

Patients with Eisenmenger syndrome should generally be given the following advice.

- Take medication only after consultation with your physician
- Avoid dehydration
- Avoid smoking
- Tell your ACHD cardiologist whether you need noncardiac surgery, or have suffered from a serious illness or injury
- Avoid excessive physical activity
- Ask to be referred to a personal physician who understands and has experience in the management of the Eisenmenger syndrome
- Avoid needless high altitude exposure, especially when combined with significant physical activity
- Flying on commercial airline flights can be safely performed with stable patients and oxyhemo-globin saturation on room air greater than 85%

Grade: Consensus
References: 87,88,90

Part V – Interventional options

Eisenmenger patients should have a hemoglobin and hematocrit level inversely proportional to their saturation level. Excessive phlebotomy or blood loss may result in a suboptimal hemoglobin level for these patients. Phlebotomy with fluid replacement with or without iron supplementation should be performed only in patients who are symptomatic from erythrocytosis. Prevention of iron deficiency is important (Section XVI – Management of Cyanotic Patients).

Grade: C
Level: V
References: 88,91,92

Supplemental oxygen at home may reduce episodes of dyspnea, although its routine use is not recommended because its effect on survival remains unclear. Psychological dependence may develop.

Grade: Consensus
References: 93

Transplantation: When patients are severely incapacitated from severe hypoxemia or congestive heart failure, the main intervention available is lung (plus repair of the cardiac defect) or heart-lung transplantation. This is generally reserved for those individuals without contraindications thought to have a one-year survival of less than 50%. Such assessment is fraught with difficulty because of the unpredictability of the time course of the disease and the risk of sudden death. The one-year survival rate for adults undergoing lung transplantation with primary intracardiac repair is 70% to 80%, with less than 50% of patients alive four years after transplantation (94-97). The outcome after heart-lung transplantation is no better, with a one-year survival rate of 60% to 80% and a 10-year survival rate of less than 30% (94,96). These options, however sobering, may be relatively attractive to individuals confronting death and those having an intolerable quality of life.

Investigational therapy – *Calcium channel blockers:* The chronic use of nifedipine in a small group of patients with Eisenmenger syndrome demonstrated a small but significant increase in exercise tolerance (98) and a decrease in pulmonary vascular resistance, especially in children (99). This therapy is still considered to be investigational and should only be prescribed in a clinical research setting.

ACE inhibitors: Data available on a highly selected group of 10 patients with cyanotic congenital heart disease showed no change in oxygen saturation despite a subjective improvement in functional capacity (100). Proponents of the use of ACE inhibitors in these patients argue that by decreasing systemic vascular resistance one improves the cardiac output and thus oxygen delivery. The counter-argument is that these agents are potentially dangerous because they lower systemic vascular resistance without changing pulmonary vascular resistance and lead to an increase in right-to-left shunting. The use of this medication remains highly experimental and should only be administered within the boundaries of a study trial guided by rigorous monitoring.

Prostacyclin: A recent study of chronic prostacyclin administration in such patients showed improvement in hemodynamics (lower pulmonary vascular resistance and increased cardiac output) and a somewhat increased exercise capacity (101). Further research in this field is needed before recommendations on the use of prostaglandins in these patients can be made.

Pulmonary artery banding: Pulmonary artery banding in one acyanotic patient with biopsy-proven pulmonary vascular changes led to regression of pulmonary vascular changes, which made surgical closure of the defects possible (102). Further data regarding this revolutionary practice are needed.

Part VI – Pregnancy

Pregnancy should be avoided. If it occurs, early termination is advised. If pregnancy is continued, maternal mortality approaches 50% with each pregnancy and fetal loss is similar. Contraception is extremely important in female patients. Sterilization (by means of laparoscopy) is generally preferred (but is not without risks), and should be conducted with skilled anesthetic and intensive care support after full consultation with the patient. Intrauterine contraceptive devices and the combined oral contraceptive pill are best avoided, although progesterone-only pills and depot injection may be acceptable after the adolescent period.

Grade: C
Level: V
Reference: 87

Part VII – Follow-up

All patients with Eisenmenger syndrome should be cared for by an ACHD cardiologist. These patients require expert supervision because of the precarious hemodynamics. They may also benefit from the involvement of other specialists within such an ACHD centre (nursing, respirology, psychology and/or psychiatry, hematology, gynecology, anesthesia, intensive care, social work).

Yearly clinical visits with complete blood count, ferritin, clotting profile, renal function, uric acid and echocardiography are recommended.

Endocarditis prophylaxis is recommended.

Grade: Consensus

TABLE 1
Cyanotic lesions

Isolated shunts with Eisenmenger physiology
Ventricular septal defect
Atrial septal defect
Patent ductus arteriosus
Aortopulmonary window
Complex lesions without Eisenmenger physiology
Complete transposition of the great arteries (PHT possible)
Truncus arteriosus (PHT possible)
Tetralogy of Fallot
Tetralogy of Fallot with pulmonary atresia (PHT possible)
Univentricular heart (PHT possible)
Tricuspid atresia
Ebstein's anomaly with atrial septal defect
Complete atrioventricular canal defect (PHT possible)

PHT Pulmonary hypertension

XVI – MANAGEMENT OF CYANOTIC PATIENTS

Part I – Background information

Cyanosis is a bluish discoloration of the skin and mucous membranes resulting from an increased amount of reduced hemoglobin. Central cyanosis in patients with congenital heart disease occurs when persistent venous to arterial mixing occurs secondary to a right-to-left shunt, resulting in chronic hypoxemia. In the presence of hypoxemia, adaptive mechanisms increase oxygen delivery. These include an increase in oxygen content, a rightward shift in the oxyhemoglobin dissociation curve and an increase in cardiac output. Oxygen delivery is enhanced at the cost of a higher hematocrit as erythropoietin production is stimulated.

Cyanosis is observed in *unoperated and palliated patients with cyanotic lesions*. Cyanotic lesions are summarized in Table 1, and palliative shunts aimed at increasing pulmonary blood flow are described in Appendix III (103,104).

Part II – History and management of unoperated patients

Adult survival into the seventh decade, although rare, is documented in cyanotic patients (105,106). Survival is determined by two factors: the underlying cardiac condition and its repercussion on the heart and pulmonary circulation; and the medical complications of cyanosis. When cyanosis is not relieved, chronic hypoxemia and erythrocytosis result in hematological, neurological, renal and rheumatic complications (107).

The hematological complications of chronic hypoxemia are erythrocytosis, iron deficiency and bleeding diathesis (108). Erythrocytosis is different from polycythemia, which is the result of an increase in cellular mass, not only of red blood cells, but also of white blood cells and platelets. Erythrocytosis may cause hyperviscosity symptoms, including headaches, faintness, dizziness, fatigue, altered mentation, visual disturbances, paresthesias, tinnitus and myalgias. Symptoms are classified as mild to moderate when they interfere with only some activities, or they can be marked to severe when they interfere with all or most activities. Individual patients have the same symptoms each time they occur. They are relieved by phlebotomy to an appropriate hematocrit level. In the iron-replete state, moderate to severe hyperviscosity symptoms may occur, typically when hematocrit levels are in excess of 65%.

With symptoms of hyperviscosity, in the iron-replete state and in the absence of dehydration, 250 to 500 mL of blood should be removed over 30 to 45 min with concomitant quantitative volume replacement with normal saline or dextran. The procedure may be repeated every 24 h until symptomatic improvement occurs.

Grade: C
Level: V
References: 108,109

Hemostatic abnormalities have been documented in cyanotic patients with erythrocytosis and can occur in up to 20% of patients. Bleeding tendency can be mild and superficial, leading to easy bruising, skin petechiae or mucosal bleeding, or the bleeding can be moderate or life-threatening with epistaxis, hemoptysis or postoperative bleeding (108). An elevated prothrombin and partial thromboplastin time; decreased levels of factors V, VII, VIII and IX; and thrombocytopenia, qualitative and quantitative platelet disorders have all been described. Findings analogous to type II von Willebrand's disease with absence of the largest vWF multimers are described. Hemostatic defects correlate with erythrocytosis. The management of bleeding diathesis is determined by the clinical circumstance, the severity and the abnormal hemostatic parameters.

- Acetylsalicylic acid, heparin and warfarin should be avoided unless indicated for chronic atrial fibrillation, the presence of a mechanical prosthetic valve or pulmonary embolus. Platelet transfusions, fresh frozen plasma vitamin K, cryoprecipitate and desmopressin can be used to treat severe bleeding
- It is recommended that cyanotic patients having surgery undergo prophylactic phlebotomy to reduce the hematocrit to less than 65%. When specific factor deficiencies are documented, fresh frozen plasma can be used as a substitute for volume replacement during prophylactic preoperative phlebotomy
- Chronic oxygen therapy is unlikely to benefit hypoxemia secondary to right-to-left shunting in the setting of a fixed pulmonary vascular resistance, and may result in mucosal dehydration with an increased incidence of epistaxis. It is, therefore, not routinely recommended

Grade: C
Level: III
References: 103,108-110

Iron deficiency is a common finding in cyanotic adult patients, occurring because of phlebotomy or excessive bleeding. Although normochromic erythrocytosis is not usually symptomatic at hematocrit levels of less than 65%, iron deficiency may manifest as symptoms similar to hyperviscosity at hematocrits well below 65% (111).

If iron deficiency anemia is confirmed, iron replacement should be prescribed.

Grade: C
Level: III
References: 108

Neurological complications, including cerebral hemorrhage, can occur secondary to hemostatic defects and can be seen following the use of anticoagulant therapy. Patients with right-to-left shunts may be at risk for paradoxical cerebral emboli. Brain abscess should be suspected in a cyanotic patient with a new or different headache or any neurological symptoms (112,113). Attention should be paid to the use of air filters in peripheral and/or central lines to avoid paradoxical emboli through a right-to-left shunt.

Renal dysfunction can manifest itself as proteinuria, hyperuricemia or renal failure (114). Increased blood viscosity from erythrocytosis in combination with arteriolar vasoconstriction can lead to renal hypoperfusion with progressive glomerulosclerosis. Hyperuricemia is common and is thought to be due mainly to the decreased reabsorption of uric acid rather than to overproduction from erythrocytosis. Urate nephropathy, uric acid nephrolithiasis and gouty arthritis are rare but may occur.

Rheumatological complications include gout and hypertrophic osteoarthropathy, which are thought to be responsible for the arthralgias and bone pain affecting up to one-third of patients.

Gallstones composed of calcium bilirubinate and consequent cholecystitis occur with increased frequency in adults, adolescents and children.

- Hydration before procedures involving contrast media should be prescribed to avoid renal dysfunction
- Asymptomatic hyperuricemia should not be treated. Long term therapy aimed at lowering uric acid levels has not been shown to prevent renal disease or gout
- Symptomatic hyperuricemia and gouty arthritis can be treated as necessary with colchicine, probenecid, sulfinpyrazone or allopurinol
- Nonsteroidal anti-inflammatory drugs should be avoided to prevent bleeding events

Grade: C
Level: V
References: 107,115

Part III – Diagnostic work-up

An initial diagnostic work-up should:

- Establish the cause of cyanosis and the source of right-to-left shunting
- Document the anatomy of underlying cardiac anomaly and palliative intervention when applicable
- Document the hemodynamic consequences of the lesion
- Document the presence or absence and degree of pulmonary hypertension
- Determine whether the patient may benefit and/or is eligible for intervention
- Document the presence or absence of the medical complications of cyanosis, and determine whether medical therapy is needed

The diagnostic work-up should include:

- In addition to a full cardiac history, a history documenting the presence or absence of symptoms of hyperviscosity, a functional inquiry pertinent to bleeding diathesis, neurological complications, renal dysfunction, gallstones and arthritis should be obtained. The functional capacity and its change over time should be documented
- An oxygen saturation level at rest in all patients and with exercise if resting saturation is greater than 90%
- 12-lead ECG
- Chest x-ray
- Baseline complete blood count, ferritin, clotting profile, renal function and uric acid
- Echocardiography Doppler evaluation by an appropriately trained individual
- Cardiac catheterization with a pulmonary vascular study and coronary angiography in patients over the age of 40 years when surgical intervention is considered
- MRI for unrestricted anatomical visualization, with cine imaging and velocity mapping for investigation of shunt lesions

Part IV – Indication for intervention

Interventions have the goal of either prolonging life or improving symptoms. There exists controversy as to whether a cyanotic adult survivor who is stable, but eligible for complete physiological repair, should be considered for surgery to improve or prolong life. Outcome varies widely and depends on the lesion and the surgical expertise and support. Symptomatic patients may manifest worsening cyanosis and ensuing medical complications, or decreasing functional capacity with or without the occurrence of symptomatic arrhythmias.

- Patients with symptoms of worsening cyanosis, decreasing functional capacity or symptomatic arrhythmias should be considered for intervention
- Eligible cyanotic patients should be considered for complete physiological repair by congenital heart surgeons
- Advanced pulmonary vascular obstructive disease with a resistance that is fixed in combination with the absence of left-to-right shunting render a patient ineligible for cardiac repair. These patients may be candidates for a palliative procedure or transplantation

Grade: Consensus

Part V – Interventional options

Percutaneous closure of intracardiac shunts: A variety of devices can be used to close ASDs, PDAs and occasionally VSDs (Sections I, II and IV).

Palliative surgical interventions: Palliative surgical interventions performed in patients with cyanotic lesions are defined as operations that serve to increase or decrease pulmonary blood flow while allowing a mixed circulation and cyanosis to persist. Palliative surgical shunts aimed at increasing pulmonary blood flow are summarized in Appendix III.

Physiological repair: Physiological repair is a term that can be applied to procedures that result in total or near-total anatomical and physiological separation of the pulmonary and systemic circulations in complex cyanotic lesions, thereby resulting in relief of cyanosis. These are described throughout this document with reference to specific lesions.

Transplantation: Transplantation of the heart, one or both lungs with surgical shunt closure and heart-lung transplantation have been performed in cyanotic patients with or without palliation who are no longer candidates for other forms of intervention. Pulmonary vascular obstructive disease precludes isolated heart transplantation, but an increasing number of patients with previous palliation and ventricular failure are successfully undergoing cardiac transplantation (116). Technical difficulties relate to previous thoracotomies and bleeding tendency in addition to intracardiac and pulmonary anatomical distortion from previous intervention.

Part VI – Interventional outcomes

Palliative surgical interventions: Systemic arterial-to-pulmonary artery shunts result in improved saturation levels with high levels of pulmonary blood flow (117,118). The long term complications of these shunts may include pulmonary hypertension, pulmonary artery stenosis and volume overload of the systemic ventricle, often making further surgical intervention more difficult or impossible. This is particularly true of large central shunts, the Potts shunt and the Waterston anastomosis. Blalock-Taussig shunts result in more controlled pulmonary flow but may stenose over time and can distort the pulmonary artery anatomy (118). Pulmonary artery banding can lead to distortion of the pulmonary artery complicating later repair.

Transplantation: The results of cardiac transplantation in properly selected patients with congenital heart disease, with and without previous palliative surgery, have improved in recent years (116). Lung transplantation (single or double) (119), with intracardiac repair can be effective in reducing pulmonary hypertension.

Part VII – Arrhythmias

Patients with Eisenmenger syndrome are at risk for sudden cardiac death, the etiology of which remains poorly defined (120). Multiple factors including arrhythmias have been described. In cyanotic patients, arrhythmias can be supraventricular or ventricular. In patients with poor ventricular function, both are poorly tolerated. The presence of atrial flutter and/or fibrillation increases the risk of paradoxical emboli and stroke. The choice of antiarrhythmic drugs are complicated by the presence of ventricular dysfunction and lung disease. In addition, there have been no drug trials in this patient population to determine possible proarrhythmic effects. The use of pacemakers to treat bradyarrhythmias, which are primary or secondary to antiarrhythmic therapy, can be complicated by inadequate venous access. The decision to use anticoagulants in patients with cyanosis is complicated by the presence of bleeding diathesis, and difficulty obtaining a true measure of international normalized ratio (INR) due to reduced plasma volume. The use of implantable defibrillators for symptomatic malignant ventricular arrhythmia has not been studied in this patient population.

- Sinus rhythm should be maintained whenever possible
- Asymptomatic ventricular ectopy should not be treated with antiarrhythmic therapy
- Reversible hemodynamic lesions should be addressed to minimize arrhythmia occurrence
- Symptomatic arrhythmias should be treated with individualized antiarrhythmic therapy
- An implantable defibrillator may be considered in patients with syncope and documented concurrent ventricular arrhythmia. Epicardial leads should be used
- Patients with atrial fibrillation should receive warfarin therapy with judicious monitoring of INR levels

Grade: C
Level: V
References: 108

Part VIII – Pregnancy

Pregnancy in cyanotic congenital heart disease, excluding Eisenmenger's reaction, results in a 32% incidence of maternal cardiovascular complications and a 37% incidence of prematurity. Pregnant women with an oxygen saturation greater than 85% fare better than women with an oxygen saturation less than 85% (121).

Part IX – Follow-up

All cyanotic patients should be followed up by an ACHD cardiologist, and particular attention should be paid to:

- Symptoms of hyperviscosity
- Systemic complications of cyanosis
- Change in exercise tolerance
- A change is saturation levels
- Occurrence of arrhythmias
- Cardiovascular risk modification and surveillance for acquired cardiovascular diseases
- Endocarditis prophylaxis
- Perioperative assessment for noncardiac surgery

In stable cyanotic patients, yearly follow-up is recommended and should include yearly blood work (complete blood count, ferritin, clotting profile, renal function, uric acid) and echocardiography Doppler studies.

APPENDIX I
Canadian Adult Congenital Heart Network centres and contact persons

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APPENDIX II
Levels of evidence used in developing the management recommendations for adults with congenital heart disease

Level of evidence	Grade of recommendation
Level I: Large randomized trials with clear-cut results and low risk of error	A
Level II: Randomized trials with uncertain results and/or moderate to high risk of error	B
Level III: Nonrandomized studies with contemporaneous controls	C
Level IV: Nonrandomized studies with historical controls	C
Level V: Case series without controls	C

APPENDIX III
Shunts (palliative surgical interventions to increase pulmonary blood flow)

Systemic venous-to-pulmonary artery shunts	
Classic Glenn	Superior vena cava to right pulmonary artery
Bidirectional Glenn	Superior vena cava to right and left pulmonary arteries
Bilateral Glenn	Right and left superior vena cava to right and left pulmonary arteries, respectively
Systemic arterial-to-pulmonary artery shunts	
Classic Blalock-Taussig	Subclavian artery to ipsilateral pulmonary artery (end-to-side)
Modified Blalock-Taussig	Subclavian artery to ipsilateral pulmonary artery (prosthetic graft)
Potts' anastomosis	Descending aorta to left pulmonary artery
Waterston shunt	Ascending aorta to right pulmonary artery

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