

# Ventricular septal defect

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Ventricular septal defects account for up to 40% of all congenital cardiac malformations. The diagnosis encompasses a broad range of anomalies, including isolated defects and those associated with other congenital cardiac malformations. Presentation, symptoms, natural history, and management of ventricular septal defects depend on size and anatomical associations of the anomaly, patient's age, and local diagnostic and interventional expertise. In this Seminar, we describe the anatomical range of ventricular septal defects and discuss present management of these malformations. Genetic determinants, diagnostic techniques, physiological considerations, and management challenges are examined in detail. Unfortunately, in many circumstances, evidence on which to guide optimum management is scarce. We present some longer term considerations of ventricular septal defects in adolescents and adults, with particular emphasis on patients with raised pulmonary vascular resistance and Eisenmenger's syndrome.

## Introduction

Ventricular septal defect is one of the commonest congenital malformations of the heart, accounting for up to 40% of all cardiac anomalies.<sup>1</sup> Frequency of this defect varies with age at examination, since many small malformations present at birth close shortly afterwards; it is also dependent on sensitivity of the examination technique. Prevalence in newborn babies of up to 5% has been reported from screening with highly sensitive colour doppler echocardiography.<sup>2</sup> Most are tiny muscular defects that disappear during the first year of life.

Since many patients can be asymptomatic, and many anomalies close with time, the precise prevalence of ventricular septal defect within populations varies between studies, depending on mode of diagnosis and age of the population. In reports in which echocardiography was used in the diagnostic algorithm, a prevalence of up to 3.94 per 1000 patients has been recorded, which is greater than in previous work that relied on either clinical examination or post-mortem investigations.<sup>3,4</sup>

Ventricular septal defect is not only a common isolated cardiac malformation but also an intrinsic component of several complex malformations, including tetralogy of Fallot or univentricular atrioventricular connection. It might also be associated with lesions, including transposition of the great arteries, congenitally corrected transposition, and aortic coarctation or interruption. However, in this Seminar we will concentrate on patients for whom ventricular septal defect is the predominant malformation.

## Genetics and cause

Our understanding of the origins of ventricular septal defect is limited by our knowledge of mechanisms that lead to normal cardiac septation. At present, information suggests that the septum has both mesenchymal and muscular components.<sup>5</sup> The mesenchymal element originates mainly from fusion of the conotruncal and atrioventricular endocardial cushions. Mechanisms that initiate development of the muscular septum are less well defined, and at least two processes have been proposed. Some researchers postulate that the muscular septum forms from coalescence of the part of the ventricular wall

that is interposed between the enlarging free walls of the developing right and left ventricles, therefore, as the ventricular cavities become deeper the septum grows passively inwards.<sup>6</sup> An alternative hypothesis suggests that the muscular septum originates from a cluster of cells, the so-called primitive interventricular septum, which expands actively towards the cushions of the atrioventricular canal.<sup>7</sup>

Several factors probably lead to development of ventricular septal defects. Failure of complete formation of the primitive interventricular septum could contribute to trabecular defects, although many muscular defects in the trabecular septum probably result from excessive undermining beneath and between trabeculae, during formation of the trabecular part of the septum. Failure of fusion of the atrioventricular cushions—with each other or with the primary septum—could result in an inlet defect, whereas malalignment or poor development of outlet cushions might add to outlet defects. Finally, failure of complete closure of the area that forms the membranous septum, in association with incomplete development of components of the muscular septum, could contribute to a perimembranous defect.

Most forms of congenital heart disease, including ventricular septal defect, have multifactorial origins.<sup>8,9</sup> An underlying inherited genetic predisposition could act synergistically with epigenetic factors, direct and indirect environmental causes, and purely stochastic effects to produce cardiac anomalies.

Monogenic defects are, in some cases, clearly causative.<sup>8</sup> Such defects have attracted much interest

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## Search strategy and selection criteria

We searched PubMed with the term "ventricular septal defect". We mainly selected publications from the past decade but did not exclude commonly cited references and highly regarded older publications. In view of recent advances in management of patients with Eisenmenger's syndrome, we undertook a separate search of PubMed with the term "Eisenmenger syndrome". Further, we reviewed reference lists of articles identified from these searches and selected those we judged especially relevant.

because their molecular characterisation has facilitated identification of important constituents of signalling pathways that govern cardiac development.<sup>10–12</sup> Mutations in the transcription factors TBX5 and GATA4 have received particular attention. These factors are coexpressed in the heart and their interaction is vital for normal cardiac septation.<sup>13</sup> TBX5 is expressed not only in the heart but also in the upper limb buds and eyes. The mutation reported most often in this transcription factor is associated with the autosomal dominant Holt-Oram syndrome,<sup>14,15</sup> characterised by abnormalities of forelimbs and several cardiac malformations, including ventricular septal defect. A TBX5 polymorphism is also associated with ventricular septal defect (without limb abnormalities) in the Chinese Han population.<sup>16</sup> Researchers have identified GATA4 sequence variants in familial cases of septal defects (particularly atrial) and in some patients with sporadic ventricular septal defect.<sup>17–20</sup>

Environmental factors such as teratogens, maternal infections, and untreated maternal metabolic illnesses (eg, phenylketonuria and pregestational diabetes) have been associated with ventricular septal defect.<sup>21</sup> Purely stochastic events could also have an important role. Cardiac development is very elaborate, requiring precise operations for successful completion,<sup>22,23</sup> which are likely to malfunction occasionally.

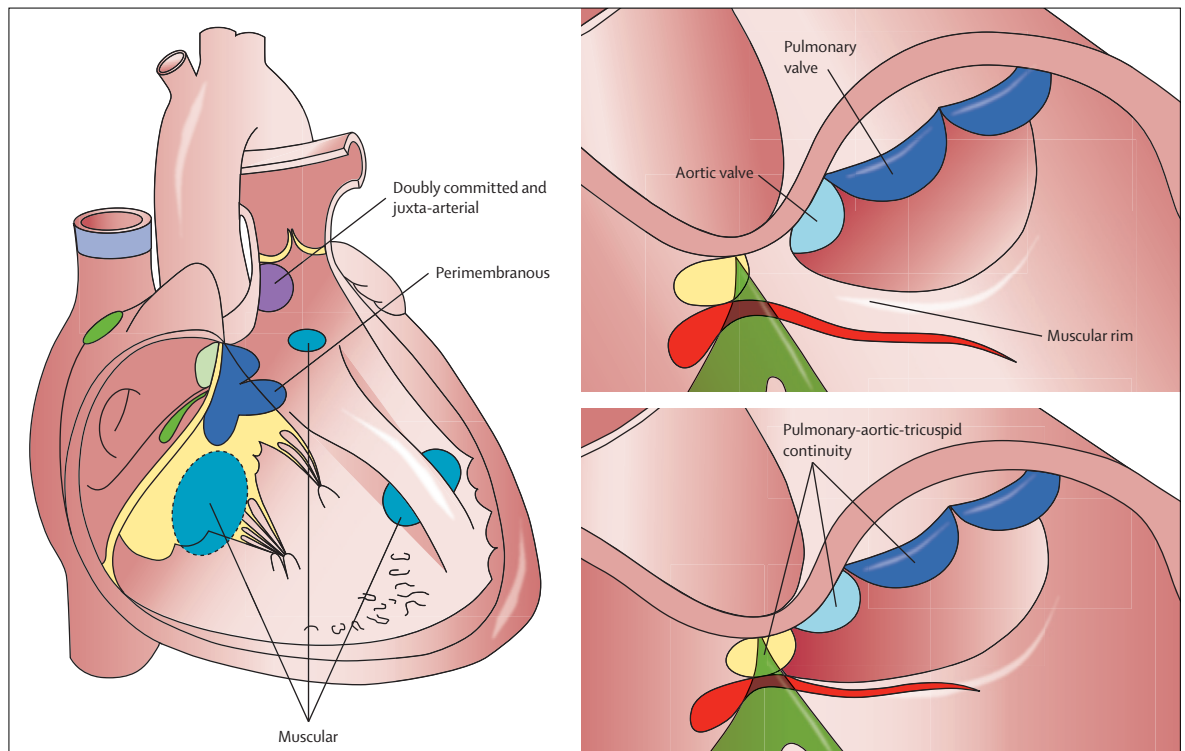
## Anatomy

Ventricular septal defect, in many respects, can be deemed one of the simpler forms of congenital malformation of the heart. However, no universal consensus exists for its classification.<sup>24–27</sup> To be brief, we will present one system to describe the anatomy of ventricular septal defects because we believe the controversy surrounding these descriptors is beyond the scope of this Seminar.

Broadly speaking, defects can be classified according to their location, either within the muscular septum (muscular defects) or at its margins. Ventricular septal defects at the margins of the muscular septum can be related to hinge-points of the leaflets of the atrioventricular valves (perimembranous), those of the arterial valves (juxta-arterial or subarterial), or both (figure 1).<sup>28</sup>

Muscular defects are located within the muscular septum. They are surrounded exclusively by muscular rims and, when viewed from the cavity of the right ventricle, can open into the right-ventricular inlet, outlet, or apex.

Perimembranous defects open into the right ventricle where the subpulmonary outflow tract turns superiorly relative to the atrioventricular junction. Such malformations are characterised by presence of fibrous continuity between leaflets of the tricuspid and aortic valves. They can extend to open into either the inlet or outlet of the right ventricle (resulting in deviation of the



**Figure 1: Location of various types of ventricular septal defect**

(Left) Location of defects viewed from the right ventricle. (Upper right) Typical doubly committed and juxta-arterial defect. (Lower right) Doubly committed, juxta-arterial, and perimembranous defect. Modified from reference 28 with permission of Elsevier.

outlet septum) or they might be large enough to open to all parts of the ventricle, the so-called confluent defect.

Doubly committed and juxta-arterial defects (also referred to as subarterial or supracristal defects) are found in an area that, in the normal heart, constitutes a freestanding tube of muscular tissue—the muscular infundibulum, which supports the pulmonary valve. An anomaly in this region will result in characteristic continuity between aortic and pulmonary valves. Most usually, these malformations have a posteroinferior rim of muscle, although they can extend into the perimembranous zone; thus, fibrous continuity also arises with the tricuspid valve, the so-called doubly committed and juxta-arterial and perimembranous defect (figure 1).

### Pathophysiology

Several key components determine the pathophysiological response to a ventricular septal defect. Primary factors are the amount and direction of interventricular shunting and the degree of volume loading to the cardiac chambers. Secondary effects include prolapse of the aortic valve and obstruction to the pulmonary or systemic outflow tract.

The amount of interventricular flow is determined by the size of the defect and relative resistances of pulmonary and systemic vascular beds. Small malformations themselves, so-called restrictive defects, provide intrinsic resistance to flow. The size of flow through larger non-restrictive defects is determined by relative resistances of pulmonary and systemic vascular beds. No agreed precise criteria exist for definition of a non-restrictive defect, although various cutoffs have been proposed, according to cross-sectional area of the defect versus area of the aortic orifice, diameter relative to body surface area, or velocity of flow across the malformation.

When a defect is non-restrictive, major determinants of the resultant interventricular flow and symptoms are relative resistances of the pulmonary and systemic vascular beds. Importantly, this relation can be very variable and dependent, in particular, on age of the patient. Left-to-right shunting might initially be minimal in babies, with fairly large defects due to high pulmonary vascular resistance characteristic of the early neonatal period. As pulmonary vascular resistance falls, left-to-right interventricular shunting rises and the patient becomes increasingly symptomatic due to excessive pulmonary blood flow.<sup>29</sup>

In some patients with ventricular septal defects, pulmonary vascular disease can develop in later childhood or in early adult life. In a few individuals, the typical postnatal decline in pulmonary vascular resistance could be delayed or arrested in the presence of a ventricular septal defect; therefore, they might never develop symptoms attributable to excessive left-to-right shunting and only present at a later stage with signs of pulmonary vascular disease. If a large lesion is left uncorrected then, over time, the amount of interventricular left-to-right shunting could decrease

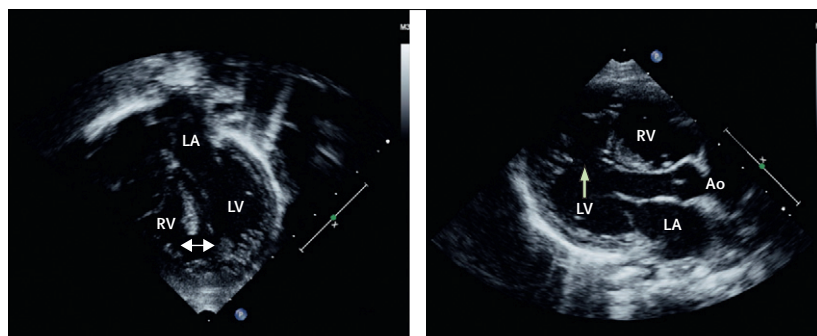
and, eventually, its direction might reverse, leading to cyanosis and Eisenmenger's syndrome.<sup>30,31</sup>

Eisenmenger's syndrome—resulting from chronic elevations of pressure and flow—is associated with functional and structural alterations within the pulmonary vasculature.<sup>32,33</sup> Key functional modifications are increased pulmonary vasoreactivity and resistance and structural microvascular changes, which include medial hypertrophy, migration of smooth muscle distally into typically unmuscularised microvessels, and ultimately, formation of so-called plexiform lesions.<sup>34</sup> Abnormalities within the endothelium contribute to all stages of this progression. Activation of endothelial-dependent vasoconstrictor pathways and aberrations of endogenous endothelium-dependent vasodilator processes play a part in functional and structural remodelling, both in animal models of shunt-related pulmonary vascular disease<sup>35,36</sup> and in the clinical condition.<sup>37</sup>

In patients with large ventricular septal defects without pulmonary vascular disease, a rise in volume loading of the left atrium and ventricle (due to increased pulmonary blood flow and, in turn, augmented pulmonary venous return) results in left heart dilation throughout the cardiac cycle. In response to the amplification in wall stress, eccentric left-ventricular hypertrophy develops. Presence of relevant longstanding pulmonary hypertension could ultimately lead to right-ventricular hypertrophy and dilation. These features will predominate as a patient enters the terminal stages of severe Eisenmenger's syndrome, which is characterised typically by pending or actual right heart failure.

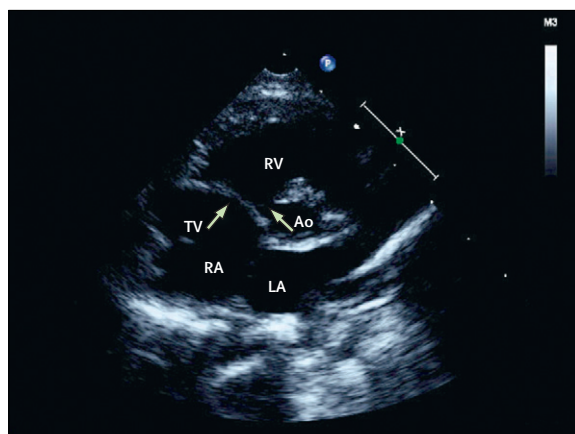
Secondary structural cardiac anomalies could contribute substantially to the clinical course of patients with ventricular septal defects. Continued surveillance of all affected individuals is essential to monitor development of these defects, because they can affect clinical management. Malformations located near the aortic valve (doubly committed, perimembranous, or muscular) can be complicated by aortic-valve prolapse and regurgitation, which result from generation of Venturi forces, in which the high-velocity jet sucks the leaflet of the aortic valve into the restrictive defect.<sup>38</sup> Several additional mechanisms could contribute to this effect, including absence of structural support for leaflets and abnormal commissural suspension.

Mid-cavity obstruction of the right ventricle due to hypertrophy of muscle bands creates the entity known as double-chambered right ventricle. This process results in formation of a proximal high-pressure chamber and a distal low-pressure chamber within the cavity of the right ventricle.<sup>39</sup> In some patients, modest anterior deviation of the outlet septum can happen. The reported prevalence of double-chambered right ventricle in individuals with ventricular septal defect varies widely within published work. An association is well recognised between double-chambered right ventricle and discrete subaortic stenosis.<sup>40</sup>



**Figure 2: Diagnosis of muscular ventricular septal defect**

Echocardiograms show apical four-chamber (left) and parasternal long-axis view (right) of a large apical muscular defect (arrows). LA=left atrium. LV=left ventricle. RV=right ventricle. Ao=aortic valve.



**Figure 3: Diagnosis of perimembranous defect**

Echocardiogram shows parasternal short-axis view of a perimembranous defect, with fibrous continuity between tricuspid (TV) and aortic (Ao) valves (arrows). RV=right ventricle. LA=left atrium. RA=right atrium.

Defects affecting the muscular outlet septum can be associated with its posterior deviation into the left-ventricular outflow tract, resulting in muscular subaortic stenosis. This malformation usually presents in early infancy and might be associated additionally with aortic coarctation or interruption.

## Diagnosis

Clinical examination can show evidence of volume loading of the left ventricle from a large ventricular septal defect, with lateral displacement of the cardiac apex. A pansystolic murmur could be present, with intensity of the murmur indicating velocity of flow across the malformation, such that smaller defects are generally loudest and can be associated with a thrill. Large anomalies—leading to an increase in mitral inflow—could generate a diastolic rumble at the apex. Patients with Eisenmenger's syndrome typically have cyanosis and clubbing, with a prominent right-ventricular heave, an accentuated pulmonary component of the second heart sound, and usually no murmur.

The electrocardiogram can be normal in patients with small ventricular septal defects. Volume loading of the left ventricle might result in left-ventricular hypertrophy, whereas raised right-ventricular pressure due to either pulmonary hypertension or obstruction to the pulmonary outflow tract could lead to right-ventricular hypertrophy.

Cross-sectional echocardiography is the mainstay of modern diagnosis of ventricular septal defect.<sup>41–43</sup> The echocardiographer will aim not only to undertake a comprehensive study of the heart—based around a sequential approach—but also to provide several key pieces of data related to the malformation, including: size and location (figure 2); anatomical relations to tricuspid, aortic, and pulmonary valves (figure 3); associated obstruction to outflow from right or left ventricles; associated prolapse of aortic valve; assessment of right-ventricular pressure; and assessment of the amount of loading of the right and left heart (left-ventricular dimension at end-systole and end-diastole should be measured and normalised for body surface area).

Integration of spectral and colour doppler with two-dimensional (2D) echocardiography greatly assists with identification and characterisation of ventricular septal defects.<sup>44–46</sup> Reliable estimates of right-ventricular and pulmonary artery pressures, and of pressure differences between left and right ventricles, can usually be obtained with 2D-directed continuous-wave doppler.<sup>47</sup> The need for cardiac catheterisation to obtain pressure data is thereby eliminated in most cases.

The echocardiographer should also assess extracardiac vascular structures, since clinically important anomalies of the aorta—especially coarctation—and pulmonary arteries, pulmonary veins, and systemic veins can be seen. Transoesophageal echocardiography has assumed an important role in intraoperative assessment of ventricular septal defect because it greatly facilitates confirmation of repair and early identification and correction of any residual lesion.<sup>48,49</sup> Three-dimensional echocardiography is becoming widely available and could provide important diagnostic assistance for assessment of unusually positioned ventricular septal defects and those associated with complex congenital heart malformations.<sup>50</sup>

Nowadays, cardiac catheterisation is undertaken rarely in patients with uncomplicated defects. This procedure is usually reserved either to measure pulmonary vascular resistance in individuals with suspected or actual pulmonary vascular disease or to close the malformation by a transcatheter approach.

MRI is used increasingly to assess patients with many forms of congenital heart disease, both before and after surgery. Although, in most individuals with ventricular heart defects, adequate diagnostic information can be obtained from clinical examination and echocardiography, MRI might be of use, particularly in patients with poor echocardiographic images.<sup>51</sup> MRI could provide additional useful information for definition of anatomy in individuals with complex defects—eg, those with

double-chambered right ventricle.<sup>52</sup> This imaging technique is especially useful for measurement of pulmonary-to-systemic flow ratio. With MRI, accurate quantification of stroke volume of both the right and left ventricles can be made.<sup>53,54</sup> Pulmonary-artery resistance can also be measured, provided simultaneous catheter or doppler determination of pulmonary-artery pressure is done.<sup>55</sup> Associated extracardiac defects, such as coarctation of the aorta and pulmonary-artery branch stenoses, which are sometimes difficult to visualise by echocardiography in older patients, can be delineated clearly.<sup>56</sup>

Fetal diagnosis of ventricular septal defect is becoming increasingly frequent as imaging techniques improve. Interest has been shown in outcomes for fetuses with malformations seen by colour flow-mapping alone in the presence of apparently normal greyscale cross-sectional imaging. In a series of 146 such fetuses, 35 had extracardiac anomalies. Of 113 babies assessed a year after birth, the defect had closed in utero in 37 and during the first year of postnatal life in 50.<sup>57</sup>

## Clinical scenarios

### Symptomatic young infant with pulmonary hypertension

A baby with such symptoms would typically become breathless with failure to thrive within the first few weeks of life. In this situation, we would usually recommend surgery within 3 months of birth. While awaiting surgery, medical treatment with low doses of diuretics with or without angiotensin-converting-enzyme inhibitors is typically used, although the evidence-base for these strategies is sparse. Monitoring of blood pressure and renal function should be done because renal failure and hypotension have been reported, particularly with angiotensin-converting-enzyme inhibitors.<sup>58</sup> The early postoperative period can be complicated by pulmonary hypertension, which results from increased pulmonary vasoreactivity after cardiopulmonary bypass. Use of inhaled nitric oxide to treat postoperative pulmonary hypertension has become widespread,<sup>59</sup> although in a Cochrane review, the paucity of data supporting its use early after cardiac surgery was highlighted.<sup>60</sup>

### Asymptomatic patient without pulmonary hypertension but with volume overloaded left heart

In this scenario, many centres would recommend closure of ventricular septal defects with the aim of avoiding potential late left-ventricular dysfunction secondary to ongoing dilation. In an observational study of 96 patients (mean follow-up almost 8 years), without any intervention, the left-ventricular end-diastolic dimension Z score fell in 29 of 33 patients and declined to less than 2 in 26 of these.<sup>61</sup> Although this series was small, the findings suggest that the optimum approach for this group of patients, who would typically be most suitable for transcatheter closure, might instead be conservative.

### Asymptomatic patient with small ventricular septal defect and no left-ventricular dilation

Much information is available from natural history studies on the long-term outlook for individuals with ventricular septal defects. Gabriel and colleagues<sup>62</sup> reported long-term outcomes in 229 patients with malformations judged “not to require surgical closure during childhood”. At a mean age of 30 years, mortality was zero, 95% were symptom-free, and left-ventricular size was normal in 89% and borderline in 10%. At the time of follow-up, four of 222 patients had experienced an episode of endocarditis. This study’s findings confirmed that with careful selection of patients, a conservative approach is warranted in this subgroup.

In a regional cohort of 290 patients with ventricular septal defect, spontaneous closure was noted in 123 of 180 cases with completely muscular borders compared with only 31 of 107 with perimembranous defects. Furthermore, muscular malformations closed spontaneously in children aged up to 88 months, whereas no perimembranous defect closed in infants older than 62 months.<sup>63</sup> Of 450 patients with perimembranous defects, at mean follow-up of 3 years, subaortic ridge developed in 26 (6%), aortic-valve prolapse in 53 (12%), and aortic regurgitation in 33 (7%).<sup>64</sup>

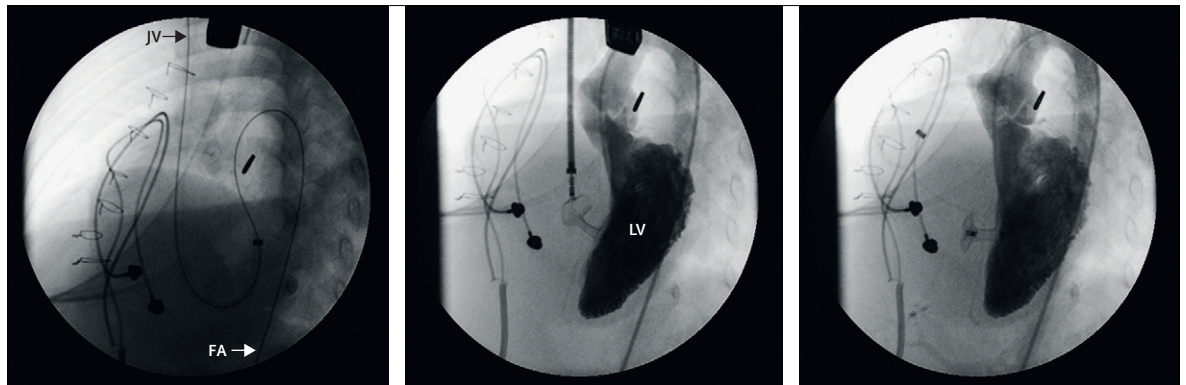
### Asymptomatic patient with small defect and prolapse or regurgitation of aortic valve

Best management for this population has historically been controversial, and up to now, no randomised trials have been published to define the optimum strategy. In an audit of patients who underwent surgery for aortic regurgitation in the setting of ventricular septal defect, those with severe preoperative regurgitation had less favourable long-term outcomes and a higher requirement for reoperation because of suboptimum valve repair.<sup>65</sup> As a result, individuals with perimembranous ventricular septal defects and more than trivial aortic regurgitation should be referred for surgery.<sup>38</sup> A reduced threshold for surgery might be justifiable in patients with juxta-arterial defects because of their high risk of aortic regurgitation and low rate of spontaneous closure.<sup>38</sup>

### Patient with Eisenmenger’s syndrome

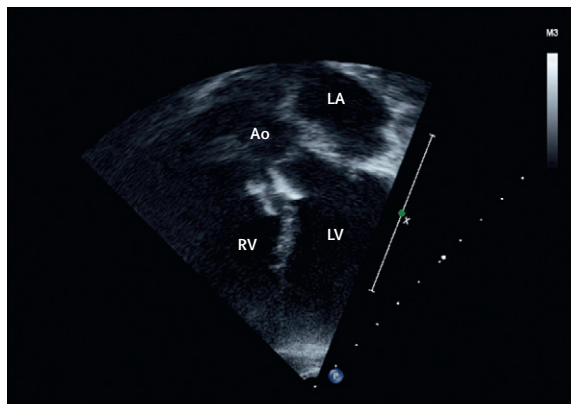
Until recent times, treatment of individuals with Eisenmenger’s syndrome was only supportive.<sup>32,66</sup> Dehydration and exposure to high altitudes should be avoided because these situations compound pre-existing hyperviscosity and arterial hypoxaemia. Historically, venesection to reduce the effects of polycythaemia was routine in many centres, although its benefits are questionable in asymptomatic patients.<sup>67</sup> Indeed, venesection can worsen iron deficiency and exercise intolerance and can amplify risk of stroke.<sup>67,68</sup> Anticoagulation has been used to manage Eisenmenger’s syndrome in the past, although supportive evidence is





**Figure 4: Transcatheter closure of muscular defect**

Patient with complex disease is paced for congenital complete heart block. (Left) A so-called railroad is created from the jugular vein (JV), across the defect, to the femoral artery (FA) to allow stable positioning of the delivery sheath. (Middle) The device is placed across the defect by advancing it through the delivery system, which has been introduced through the jugular vein. LV=left ventricle. (Right) The device is released and a ventriculogram shows it is well placed and there is no residual shunting.



**Figure 5: Percutaneous closure of a perimembranous defect**

Echocardiogram after device closure of a perimembranous defect. The device is close to the aortic valve (Ao) and the conduction axis (see figure 1). LA=left atrium. LV=left ventricle. RV=right ventricle.

scarce and bleeding risk could be considerable.<sup>69</sup> Female patients must be made aware that pregnancy is associated with substantial maternal and fetal risk (see Issues in adults with ventricular septal defects).

Recognition of the role of disrupted endothelial messengers in pathogenesis of Eisenmenger's syndrome has broadened pharmacotherapeutic options for this disorder.<sup>33</sup> Endothelial-based treatments, particularly those aimed either at blockade of the potent vasoconstrictor endothelin 1 or at prevention of catabolism of the nitric oxide-dependent vasodilator cGMP, are used increasingly in this population of patients.<sup>70–72</sup> In the BREATHE-5 study, bosentan—a dual endothelin receptor-antagonist—lengthened 6-min walk distances in a randomised placebo-controlled trial over 16 weeks<sup>73</sup> and in an open-label extension.<sup>74</sup> These improvements continued for an additional 24 weeks. Findings of an open-label study showed increases in functional capacity that were maintained, particularly in adults.<sup>75</sup> Improvements in quality of life and functional capacity were reported in patients with Eisenmenger's

syndrome in response to oral sildenafil, a phosphodiesterase inhibitor that raises cGMP levels.<sup>76</sup> Advanced endothelial-based treatments increase survival in individuals with Eisenmenger's syndrome.<sup>77</sup>

These advances, combined with the observation that many patients with Eisenmenger's syndrome are responsive to vasodilators in the catheterisation laboratory,<sup>78</sup> raise the possibility that aggressive endothelial-based treatments could restore operability in individuals who had previously been judged inoperable. Several published reports accord with this idea, although systematic studies are scarce.<sup>79</sup>

## Endocarditis

Traditionally, antibiotic prophylaxis was recommended routinely in patients with ventricular septal defects to prevent procedure-associated endocarditis. This guidance is based on recognition that such individuals are at increased risk of endocarditis, that this disorder could result from bacteraemia, that dental procedures might result in bacteraemia, and that treatment with antibiotics might reduce risk of bacteraemia and endocarditis. However, later evidence indicates that endocarditis is most likely to result from chronically poor dental hygiene and activities of daily living, which—coupled with the paucity of data in support of the effectiveness of antibiotic prophylaxis for prevention of endocarditis—has resulted in revised guidelines. These recommendations suggest that patients with uncomplicated ventricular septal defects do not need antibiotics, but they put strong emphasis on primary prevention of dental infections, with meticulous daily dental hygiene and regular dental review. However, antibiotic prophylaxis for dental and other procedures continues to be recommended for 6 months after complete surgical or transcatheter closure of a ventricular septal defect and indefinitely when a residual defect is present in relation to patch material, because this situation could inhibit endothelialisation.<sup>80</sup>

## Closure of ventricular septal defects

### Surgery

Patch closure of a ventricular septal defect through sternotomy, with cardiopulmonary bypass, has been done for more than 50 years. With enhanced selection of patients, early surgery, and advances in perioperative care, operative mortality is low and substantial postoperative morbidity is rare.<sup>81</sup> Usually, access to the defect is obtained through either the atrioventricular or semilunar valves, thus avoiding ventriculotomy. In some individuals, intraoperative temporary detachment of anterior and septal leaflets of the tricuspid valve can increase exposure of the defect.<sup>82</sup> Most patients after surgery report normal quality of life, compared with age-matched controls, although behavioural and school performance difficulties might be present in early childhood.<sup>83</sup>

With expansion of cardiac surgery to the developing world,<sup>84</sup> interest has grown in techniques to close defects in patients who did not have access to surgery in infancy, who have subsequently developed raised pulmonary vascular resistance. Surgical closure in these high-risk individuals

can result in substantial morbidity and mortality, because increases in pulmonary-arterial and right-ventricular pressure result in right-ventricular failure. A modified surgical technique with creation of a so-called valved patch, which allows unidirectional right-to-left shunting across a deliberate residual defect, can be undertaken with low operative mortality,<sup>85</sup> although the benefits of this procedure over conventional closure have been questioned.<sup>86</sup>

In the past, banding of the pulmonary artery was done frequently as an interim palliative procedure to reduce pulmonary blood flow, particularly in infants. This technique is now undertaken rarely, except in individuals with either many ventricular septal defects or apical malformations, in whom surgical access to the anomalies is anticipated to be especially difficult or impossible. Application of either absorbable or balloon-dilatable bands has been performed in patients with multiple muscular defects, which potentially could avoid the need for removal of the band if anomalies reduce in size over time.<sup>87</sup>

The main surgical challenges are with defects that are near the apex and are difficult to access through either the

	Unrepaired defect	Repaired defect
Survival	Excellent survival for small defects; large defects can be associated with pulmonary vascular disease; might develop aortic regurgitation	Excellent survival; occasional residual shunt; might develop right-ventricular or left-ventricular outflow-tract obstruction; might develop aortic regurgitation
Haemodynamic issues	Left-to-right shunt; left-ventricular dilation and impaired function; aortic regurgitation; pulmonary vascular disease	Residual shunt; ventricular function; aortic regurgitation; right-ventricular or left-ventricular outflow-tract obstruction
Arrhythmia and pacing	Rare	Rare atrioventricular block; rare ventricular block
Investigations		
Chest radiography	Cardiomegaly	Cardiomegaly
ECG	Rhythm and conduction; right-ventricular hypertrophy	Rhythm and conduction; right-ventricular hypertrophy
Echocardiography	Number and size of defects; left-ventricular and right-ventricular function; aortic regurgitation	Residual shunt; ventricular function; aortic regurgitation
Transoesophageal echocardiography	If transthoracic image is inadequate	If transthoracic image is inadequate
Cardiac catheterisation	Pulmonary vascular disease; associated lesions	Rarely needed
Holter test	Only if symptomatic	Only if symptomatic
Exercise test	If symptomatic; sports counselling	If symptomatic; sports counselling
Indications for intervention	Left-to-right shunt with heart overload; reversible pulmonary hypertension; aortic regurgitation; associated abnormalities (right-ventricular outflow tract, subaortic stenosis); previous endocarditis	Left-to-right shunt with heart overload; reversible pulmonary hypertension; aortic regurgitation; associated abnormalities (right-ventricular outflow tract, subaortic stenosis); previous endocarditis
Endocarditis prophylaxis	Not needed	If residual defect
Pregnancy	No contraindications with uncomplicated defects; contraindicated with pulmonary vascular disease	No contraindications with closed defects; contraindicated with pulmonary vascular disease
Physical exercise	No restriction for small defects	No restriction for closed defects
Follow-up care		
Aortic regurgitation	Exclusively specialist centre	Exclusively specialist centre
Complicated haemodynamics	Exclusively specialist centre	Exclusively specialist centre
Pulmonary vascular disease	Shared care between specialist centre and general adult centre	Shared care between specialist centre and general adult centre
Small defect	Managed in non-specialist centre with access to specialist centre if needed	Managed in non-specialist centre with access to specialist centre if needed

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**Table: Issues related to ongoing surveillance of patients with ventricular septal defects**

atrioventricular or semilunar valves. In some situations, malformations can be accessed through a ventriculotomy, although transcatheter approaches have been used.

### Transcatheter closure

Over the past decade or so, transcatheter techniques for closure of ventricular septal defects have been developed. These methods have been especially useful for muscular defects, which can be the most difficult to access surgically (figure 4).<sup>88</sup> Much interest has been generated in development of transcatheter approaches to close perimembranous defects (figure 5). At present, this technique is not undertaken in most units because of the unacceptably high rate of post-procedure heart block associated with currently available devices. Of particular concern is that this risk does not subside or fall with time, with late-onset heart block being fairly prevalent.<sup>89,90</sup> As softer devices are developed, this method could potentially be reintroduced in the future.

### Hybrid techniques

In infants with muscular ventricular septal defects, in whom both transcatheter and standard surgical approaches are difficult, a hybrid technique for closure has been implemented, which brings together surgery and interventional methods. With this method, a sternotomy is done in the standard way and the device is placed in the right ventricle through its anterior wall, under transoesophageal and fluoroscopic guidance.<sup>91</sup>

### Issues in adults with ventricular septal defects

#### Exercise

Adults with small ventricular septal defects, normal pulmonary arterial pressure, normal ventricular function, and no associated lesions should have a normal tolerance for exercise and, therefore, no exercise restrictions should be imposed (table).<sup>92</sup> Those with pulmonary arterial hypertension usually self-restrict their amount of exercise. In a large study of adults with congenital heart disease who underwent formal testing, patients with Eisenmenger's syndrome achieved the lowest levels of peak oxygen consumption during exercise and, furthermore, the extent of the reduction in peak oxygen consumption was an important marker of prognosis.<sup>93</sup>

#### Pregnancy

Women with small ventricular septal defects without pulmonary hypertension do not seem to be at increased cardiovascular risk during pregnancy (table). Those with moderate defects could have raised pulmonary blood flow during pregnancy, an indication of increased circulating volume, although this effect could—to a degree—be counterbalanced by reduction in systemic vascular resistance. By contrast, pregnancy in women with Eisenmenger's syndrome is associated with a very high risk of maternal and fetal death and premature delivery.<sup>94</sup>

In a study of 17 ongoing pregnancies in ten women with Eisenmenger's syndrome,<sup>95</sup> one maternal death was reported and another woman deteriorated greatly, requiring high-level intensive care. Four spontaneous abortions and one stillbirth happened. Of the 12 deliveries of live infants, ten were premature.<sup>95</sup> Against this background, women with Eisenmenger's syndrome should be counselled strongly against pregnancy and should be referred to a specialist for contraception advice.<sup>96</sup> Although sterilisation might be deemed appropriate for some women, it should only be done at a specialist centre with careful periprocedural care of these high-risk patients. Early termination is often recommended for women with Eisenmenger's syndrome who become pregnant. For those who choose to continue pregnancy, obstetric care should be undertaken at a specialist centre, with access to intensive care. Even after successful delivery, maternal risk continues beyond the time of birth; therefore, close monitoring must be maintained in the postpartum period. Data suggest that augmentation of endothelial-based treatments—eg, combination of intravenous epoprostenol and oral sildenafil—might improve outcome for pregnant women.<sup>97</sup>

#### Contributors

Both authors wrote the report and approved the final version.

#### Conflicts of interest

We declare that we have no conflicts of interest.

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