FEATURE

# Pregnancy and heart disease

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*The substantial cardiovascular adaptation that occurs during normal pregnancy may precipitate the first presentation of heart disease. A multidisciplinary approach comprising GPs, obstetricians, cardiologists, cardiac anaesthetists and neonatologists is required for the optimal management of pregnancy in women with heart disease.*

## Key points

- **Pregnancy is associated with major physiological changes resulting in an augmentation of cardiac output of 40 to 50% by the end of the second trimester.**
- **Women with pre-existing heart disease who are unable to compensate for increased cardiac demand may present with an exacerbation of their heart disease during pregnancy.**
- **Valvular heart disease, arrhythmias and congenital heart disease are the major cardiac abnormalities encountered during pregnancy in antenatal clinics.**
- **GPs caring for women peripartum are often the first to document a murmur or arrhythmia and determine the need for further investigation.**
- **Optimal management of pregnancy in women with heart disease can be achieved in antenatal clinics utilising a multidisciplinary team.**

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Pregnancy is associated with major physiological changes, including a fall in systemic vascular resistance, increased blood volume and increased heart rate, resulting in an augmentation of cardiac output of 40 to 50% by the end of the second trimester.[1-3] Further haemodynamic changes include reduced preload caused by compression of the inferior vena cava in the supine position towards the end of pregnancy; increased cardiac output and blood pressure during labour; effects of regional and general anaesthesia, particularly on blood pressure; and increased preload following autotransfusion of uterine blood after delivery.[1,2]

Women with pre-existing heart disease, who are unable to compensate for this increased cardiac demand, may present with an exacerbation of their heart disease in pregnancy. The challenge for doctors managing these women around the time of their pregnancy is to identify those who have significant heart disease, to optimise their status prior to pregnancy – usually with involvement from a range of healthcare professionals – and to reduce maternal and fetal morbidity.

This article considers women with valvular heart disease, arrhythmias and congenital heart disease, the major cardiac abnormalities encountered during pregnancy in antenatal clinics. Other cardiac diseases that may present during pregnancy, but which are outside the scope of this article, include ischaemic heart disease and associated risk factors, which are increasing in older women, aortopathy in Marfan's syndrome or associated with bicuspid aortic valves, and cardiomyopathy, which may be pre-existing or may develop during pregnancy. The following three case studies are illustrative only and composites of a number of cases. Personal details have been modified.

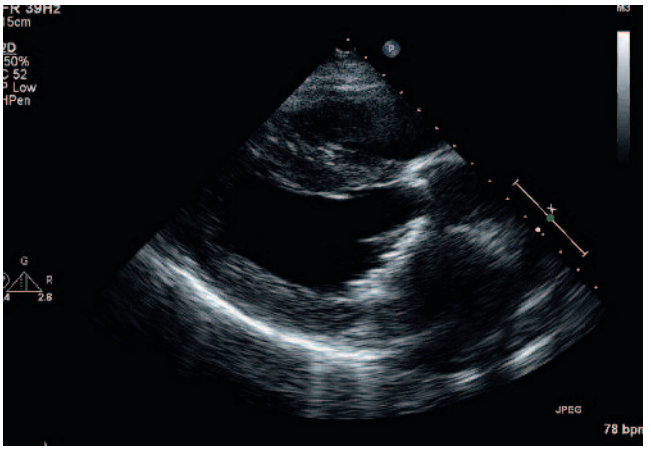


Figure 1. Parasternal long-axis echocardiography showing left ventricular hypertrophy.

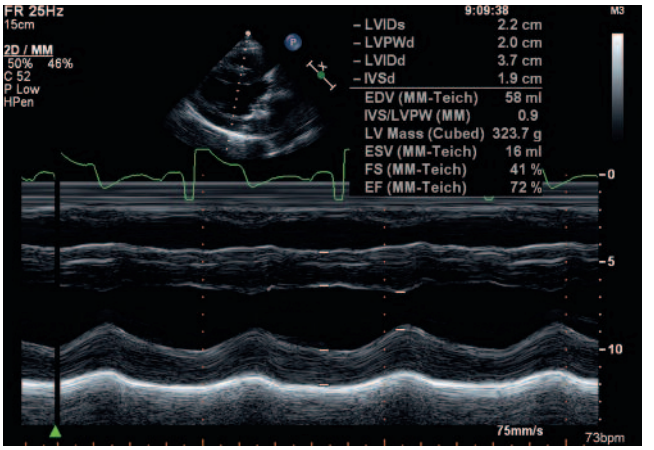


Figure 2. M-mode echocardiography showing left ventricular hypertrophy (wall thickness, 19 to 20 mm) and normal contraction (fractional shortening, 41%).

## Case 1: valve disease in pregnancy

A 24-year-old woman with a history of rheumatic fever and aortic and mitral mechanical valve replacement 14 years previously presented at six weeks of gestation. The patient had recently arrived in Australia and had not had regular medical reviews or international normalised ratio (INR) monitoring. She was also dyspnoeic after climbing one flight of stairs.

Examination revealed she had a blood pressure of 90/60 mmHg, sinus rhythm with a heart rate of 75 bpm, reduced volume carotid pulse, apex displaced and pressure overloaded, soft aortic prosthetic sounds and an aortic ejection systolic murmur. Allowing for the normal changes of pregnancy (see the box on this page), this woman had features consistent with significant aortic stenosis, with low pulse pressure and reduced volume carotid pulse, and left ventricular hypertrophy. In addition, she was taking warfarin, which is teratogenic particularly in the first trimester.

During pregnancy, as peripheral resistance decreases murmurs associated with regurgitant lesions may become softer and those associated with stenotic lesions, such as aortic stenosis, may increase. In normal pregnancy, blood pressure reduces to a nadir in the second trimester with a widened pulse pressure – and not the low pulse pressure present in this patient with severe aortic stenosis.[2] Specific features of the murmur in this patient suggest referral is required for cardiac assessment (grade 3 or greater midsystolic murmur; see the box on this page).

Of concern in this case was this patient's reduced exercise capacity in early pregnancy (New York Heart Association [NYHA] class II symptoms, mild limitation of ordinary activity), which occurred prior to the anticipated major cardiovascular changes of pregnancy. In the absence of adequate anticoagulation, and with the hypercoagulability of pregnancy, valve thrombosis was a possibility in this patient. Echocardiography confirmed severe concentric left ventricular hypertrophy with normal systolic function (Figures 1 and 2), severe aortic prosthetic stenosis (mean gradient, 71 mmHg at rest; Figure 3), a normally functioning mitral prosthesis and mild resting pulmonary hypertension (right ventricle [RV]:right atrium [RA] systolic pressure gradient, 43 mmHg). There was no thrombus evident on transthoracic study. Fluoroscopy confirmed limited opening of the aortic tilting disc valve.

The risk of the pregnancy to the mother and fetus was discussed, including the risk of sudden death, heart failure and preterm delivery (see the box on page 13). The patient made the decision to terminate the pregnancy, and proceeded to cardiac surgery.

### Normal cardiac changes in pregnancy

Examination findings that may represent normal cardiac changes in pregnancy include:

- raised jugular venous pressure
- apex displaced, volume loaded
- prominent splitting of first and second heart sounds, third heart sound
- sinus tachycardia and atrial and ventricular premature beats
- systolic aortic or pulmonary flow murmur
- continuous murmur from venous hum or mammary soufflé
- peripheral oedema

### When to investigate a pregnant patient with a murmur

Investigate further in the presence of:

- diastolic or continuous murmur
- holosystolic or late systolic murmur
- grade 3 or greater midsystolic murmur
- murmur associated with other abnormal physical findings (pulmonary hypertension, cardiac enlargement) or ECG or chest x-ray changes

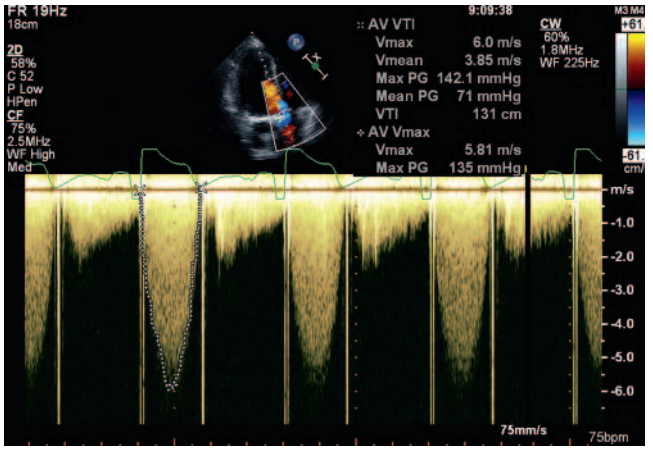


**Figure 3. Continuous wave Doppler signal showing aortic $V_{max}$ of 3.9 m/s and mean gradient of 71 mmHg.**

Subvalvular pannus and obstructive prosthetic aortic stenosis was confirmed and a replacement mechanical aortic valve inserted. The patient's exercise tolerance improved and left ventricular hypertrophy resolved. Optimal anticoagulation management was ensured under the care of her new GP.

## Anticoagulation in pregnancy

The patient and her husband later attended their GP to discuss a planned pregnancy in the setting of her prosthetic valves and warfarin therapy. Her GP highlighted the risk of valve thrombosis (9% with heparin and 4% with warfarin) and of teratogenicity with the use of warfarin.[4] Warfarin embryopathy has an incidence of 6%, and risk is highest for first trimester exposure and appears to be dose-related. There is a lower incidence of embryopathy when a daily dose of less than 5 mg warfarin is required.[4,5]

The patient elected to use enoxaparin in combination with aspirin (which confers additional antithrombotic protection) from the point of her pregnancy diagnosis to 12 weeks of gestation. Thereafter, she switched to treatment with warfarin and aspirin, and continued therapy until 36 weeks (see the box on this page).

## Treating valve disease in pregnancy

In general, treatment of significant valvular pathology is best performed before pregnancy, but this relies on accurate assessment by the GP. Definitive treatment may include percutaneous balloon mitral valvuloplasty for mitral stenosis (which can also be performed safely during pregnancy), valvuloplasty for aortic stenosis or subaortic membrane and mitral repair. Percutaneous procedures during pregnancy require measures to reduce radiation exposure and should be avoided in the first trimester.[2,6,7] The fetal mortality for cardiovascular surgery requiring cardiopulmonary bypass is almost 30%, even with high flow rates and warm perfusion temperatures. Surgery should preferably be delayed until the viability of the fetus is established and a caesarean section can be performed.[1]

### Heart disease and associated risks in pregnancy

**Heart disease associated with high maternal or fetal risk**

- Moderate to severe aortic stenosis
- Mitral stenosis with NYHA class II to IV symptoms
- Aortic regurgitation or mitral regurgitation with NYHA class III to IV symptoms
- Valve disease with left ventricular dysfunction
- Mechanical prosthetic valve requiring anticoagulation
- Peripartum cardiomyopathy

**Heart disease associated with very high maternal or fetal risk**

- Severe pulmonary hypertension
- Cyanotic congenital heart disease or Eisenmenger physiology
- Severe left heart obstruction
- Severe ventricular dysfunction
- Marfan's syndrome with aortic dilatation

Abbreviation: NYHA = New York Heart Association

### Modified ACC/AHA guidelines for alternative anticoagulation regimens in pregnancy[1]

1. Adjusted dose low molecular weight heparin (anti-Xa four hours post-dose, 0.7 to 1.2 IU/mL)
2. Aggressive adjusted dose unfractionated heparin (APTT six hours post-dose, ≥ 2 x control)
3. Low molecular weight or unfractionated heparin in first trimester, warfarin until 36 to 40 weeks of gestation (INR 2.5 to 3.5), low molecular weight or unfractionated heparin thereafter
   - Discontinue warfarin two to three weeks prior to planned delivery and change to heparin. Resume unfractionated heparin four to six hours post-delivery and recommence warfarin
   - Consider addition of aspirin (75 to 100 mg) in high-risk women in their second and third trimester

Abbreviations: ACC = American College of Cardiology; AHA = American Heart Association; APTT = activated partial thromoplastin time; INR = international normalised ratio; NYHA = New York Heart Association.

Regurgitant lesions such as mitral and aortic regurgitation are better tolerated than conditions such as aortic stenosis (in which relatively fixed cardiac output may not allow adaptation to pregnancy) and mitral stenosis (which is worsened by sinus tachycardia or atrial fibrillation, which reduce the diastolic filling time). Beta-1 selective β-blockers may be useful in patients with mitral stenosis to reduce tachycardia. Valve replacement, which carries the risk of anticoagulation for mechanical valves or early failure and reoperation for bioprosthetic valves, may on occasion be best deferred until after pregnancy.[6-8] Antibiotic prophylaxis for endocarditis is

required during labour for patients with prosthetic valves (see the box on this page).

## Case 2: palpitations in pregnancy

A 31-year-old woman at 29 weeks of gestation in her first pregnancy presented to her GP with a history of intermittent palpitations for the past month. On examination, her blood pressure was 115/70 mmHg and her heart rate was 80 bpm and rhythm regular. A late systolic murmur was heard, maximal at the apex.

Arrhythmias are common in pregnancy, particularly in women with pre-existing heart disease, and are generally benign. GPs may select when to investigate further based on markers of risk, such as structural heart disease, family history or increasing symptoms (see the box on this page). Examination must consider the range of normal cardiac changes in pregnancy (see the box on page 12) and the possible normal changes in the ECG, including frontal lead axis change and nonspecific ST-T changes found in 4 to 14% of pregnant women.[2]

Atrial and ventricular premature beats occur in 60% of pregnant women and may not be correlated with either heart disease or symptoms such as palpitations, dizziness or syncope.[9] Normal echocardiographic findings in pregnancy include mild enlargement of cardiac chambers, progressive mild increase in wall thickness, increased systolic velocities across valves and pulmonary, tricuspid and mitral regurgitation.[10]

### Endocarditis prophylaxis in pregnancy

Amoxycillin or ampicillin (2 g IV) administered prior to delivery can be used for prophylaxis of endocarditis in high-risk groups or in all patients with prolonged labour or infection. High-risk groups requiring endocarditis prophylaxis at delivery include those with:[1]

- prosthetic heart valves or prosthetic material
- previous infective endocarditis
- congenital heart disease: unrepaired cyanotic defects, completely repaired defects within six months, residual defects
- cardiac transplantation with valvulopathy
- rheumatic heart disease in Indigenous Australians

### When to investigate a pregnant patient with palpitations

Investigate further in the presence of the following markers of risk:

- structural heart disease – abnormal findings on examination or cardiac investigations
- family history – sudden cardiac death, hypertrophic cardiomyopathy, long QT interval
- increasing symptoms – presyncope, inability to continue with current activity

This patient had no significant family history of heart disease. Features on examination and echocardiography confirmed mitral valve prolapse with mild late systolic regurgitation and otherwise normal appearing mitral leaflets and normal systolic function.

Moderate mitral regurgitation is well tolerated in pregnancy because the fall in systemic vascular resistance offsets the increase in preload. During palpitations, the patient was able to continue with normal activities and had not experienced presyncope. Her ECG was normal. Holter monitoring showed sinus tachycardia to a maximum heart rate of 150 bpm, correlating with her symptoms. The patient was reassured and no medication was prescribed. Her symptoms settled over the following two weeks.

## Treating arrhythmias in pregnancy

Supraventricular arrhythmias, such as atrial tachycardia or atrioventricular junctional re-entry, may occur with increased frequency during pregnancy. Atrial fibrillation is unusual unless associated with mitral valve disease or cardiomyopathy. For supraventricular arrhythmias, treatment measures include reassurance, vagal manoeuvres, adenosine, β-blockers and direct current reversion.[2] Verapamil is a second-line agent with the potential for cardiovascular effects on the fetus, and amiodarone should not be used unless life-saving for the mother (due to potential fetal thyroid and neurological effects).[1]

Ventricular arrhythmias are uncommon in structurally normal hearts. A benign idiopathic ventricular tachycardia may arise from the right ventricular outflow tract, but this will generally respond to β-blockers and can be cured by catheter ablation after pregnancy.[2]

## Case 3: congenital heart disease in pregnancy

A 24-year-old asymptomatic woman was referred from the antenatal clinic at 28 weeks of gestation because of a murmur. Examination revealed a loud pulmonary component of the second heart sound consistent with pulmonary hypertension, a grade 3/6 pulmonary flow murmur and no evidence of heart failure.

Echocardiography showed a dilated right heart (Figure 4) with a large secundum atrial septal defect (Figure 5) and moderate pulmonary hypertension at rest. On exercise stress testing, the patient's exercise tolerance was reduced commensurate with gestation (6.25 minutes on the Bruce protocol, 7.6 metabolic equivalents [METs] achieved, 11 METs predicted). Her RV:RA pressure gradient increased from 54 mmHg at rest (Figure 6) to 73 mmHg post exercise (Figure 7).

## Managing congenital heart disease in pregnancy

Most patients with atrial septal defects tolerate pregnancy. This is because increased cardiac output in the presence of a volume-loaded RV (left to right shunt) is offset by decreased peripheral vascular resistance.[2] There is a risk of paradoxical embolism with atrial septal defects, which is increased during pregnancy and postpartum.[11]

This patient progressed well through her pregnancy with maintained exercise tolerance, only mild worsening of her pulmonary

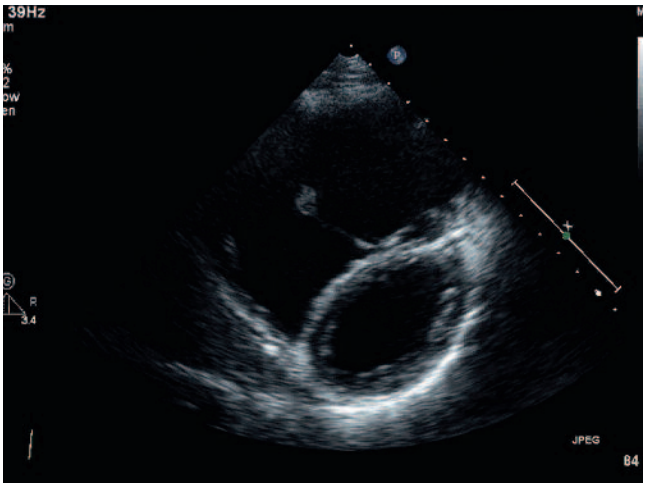


Figure 4. Parasternal short-axis echocardiography showing volume-overloaded right ventricle.

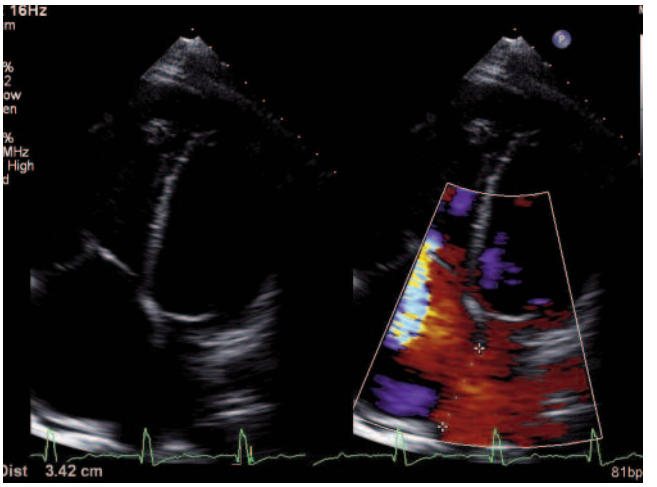


Figure 5. Apical four-chamber echocardiography showing large secundum atrial septal defect with left to right flow on colour Doppler.

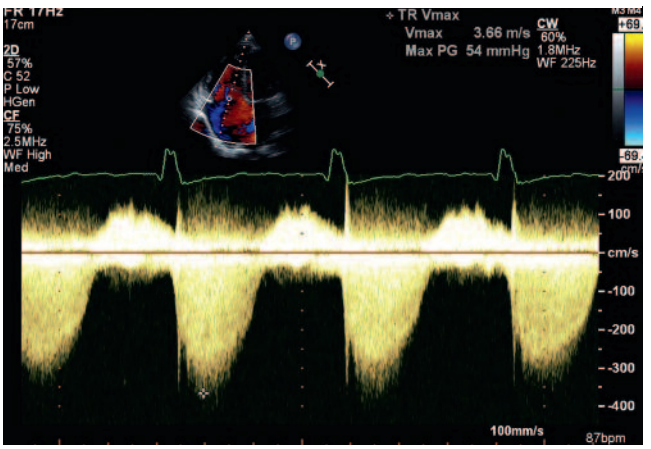


Figure 6. Resting right ventricle: right atrium pressure gradient of 54 mmHg on continuous wave Doppler.

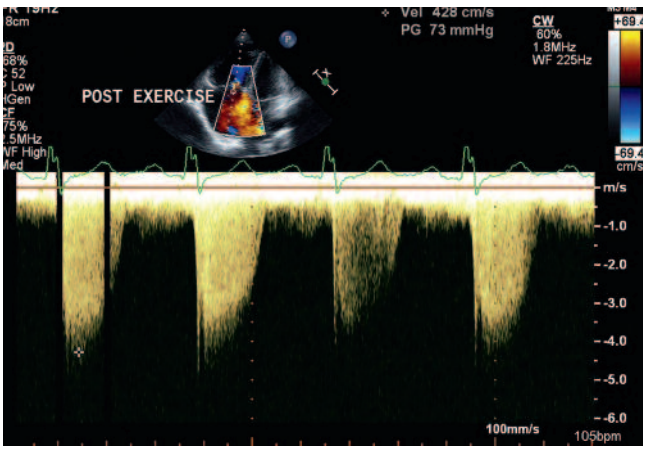


Figure 7. Post exercise right ventricle: right atrium pressure gradient of 73 mmHg.

hypertension and no evidence of heart failure. She was induced at term when the cervix was favourable (synthetic oxytocin was used at an increased concentration to reduce fluid load). Epidural anaesthesia was administered to reduce tachycardia and hypertension due to pain, and with the intention of limiting the second stage of labour if required. The requirement for antibiotic prophylaxis for endocarditis during labour in patients with congenital heart disease should be considered (see the box on page 14). A cardiology review in labour confirmed there was no development of heart failure.

Caesarean section results in greater haemodynamic changes and more blood loss than vaginal delivery, and is typically reserved for obstetric indications.[12] The first 48 to 72 hours after delivery remain a high-risk time for the patient, with return of uterine blood to the circulation and increased peripheral resistance.[13] Women with severe pulmonary hypertension (pulmonary pressure greater than or equal to two-thirds of systemic pressure) are at particularly increased risk in pregnancy, and pregnancy is not advised.

Four months following delivery, the patient underwent surgical closure of her atrial septal defect, with normalisation of her right ventricular size and pulmonary pressures. No further problems are anticipated during subsequent pregnancies, except for a higher incidence of atrial arrhythmias. There is, however, an increased risk of congenital heart disease in the children of women with congenital heart disease (overall risk of 2 to 5%, an increase of 10-fold compared with the background rate). The risk is greater in women with conditions such as ventricular septal defect (4 to 10%), bicuspid aortic valve (up to 24%) and tetralogy of Fallot (16%).[2,13] In addition to genetic counselling, women with congenital heart disease should be offered fetal echocardiography between 18 and 22 weeks of gestation.[13]

Congenital heart disease is now the most common form of heart disease in pregnant women and the incidence is increasing as children with corrected congenital heart disease survive to adulthood.[13] GPs caring for women peripartum are often the first to document

a murmur and they determine the requirement for further investigation. Morbidity in pregnancy complicated by congenital heart disease in the mother varies depending on the severity of the underlying disorder, and includes pregnancy loss (15%), heart failure (5%) and arrhythmias (5%).[14] Risk factors for cardiovascular adverse events are NYHA class II to IV, cyanosis, left ventricular ejection fraction below 40%, significant left heart obstruction and a previous cardiac event.[15]

## Conclusion

The major cardiovascular adaptation that occurs during normal pregnancy may precipitate the first presentation of cardiac disease or exacerbate existing heart disease. The optimal management of pregnancy in women with heart disease may be achieved in antenatal clinics with the assistance of a multidisciplinary team including GPs, obstetricians, cardiologists, cardiac anaesthetists and neonatologists. CT

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COMPETING INTERESTS: None.


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