Pregnancy and the heart

David Williams

Pregnancy places a huge demand on the heart. Such a burden cannot always be met by women with pre-existing heart disease. This article covers the important physiological changes of healthy pregnancy, and discusses how to assess and manage heart disease during pregnancy.

In normal pregnancy, there is an increase in heart rate and ventricular function, combined with a fall in total peripheral vascular resistance that increases maternal cardiac output (CO) as early as 5 weeks after the last menstrual period (Robson et al, 1989). By 24 weeks, CO has increased by 45%, from 4.8 litres/min to 7.2 litres/min. In the third trimester, CO falls when the gravid uterus compresses the inferior vena cava. Two weeks postpartum, CO has almost returned to pre-pregnancy levels.

Total extracellular fluid volume increases by 6–8 litres, with a relatively greater increase in intravascular compared with interstitial fluid volume. However, arterial and venous dilatation in the first trimester creates a relatively underfilled state associated with a fall in blood pressure (Redman, 1995). By 32 weeks gestation, plasma volume has reached a maximum of 40% (1.2 litres) above pre-pregnancy levels. In anticipation of haemorrhage at childbirth, normal pregnancy is characterized by low grade, chronic intravascular coagulation within both the maternal and utero-placental circulation.

CARDIOVASCULAR EXAMINATION IN PREGNANCY

History

The most frequent symptom of cardiac disease in pregnancy is dyspnoea. However, this is a variable feature of healthy pregnancy. Furthermore, syncope is also common in normal pregnancy, but can be a symptom of severe aortic stenosis or dysrrhythmias. Knowledge of the outcome of a previous pregnancy is useful.

Physical signs

The hyperdynamic circulation of pregnancy causes alterations in the cardiovascular system which mimic heart disease. The peripheral pulses are full, bounding and often collapsing, suggesting aortic regurgitation to the untutored. Premature atrial and ventricular ectopic beats are common in normal pregnancy. In late pregnancy, the jugular venous pressure may be raised as a result of increased intrathoracic pressure secondary to increased intra-abdominal pressure. The apex beat is more forceful and, because of the increase in CO, may suggest cardiomegaly in normal patients. On auscultation, the first heart sound is loud and a third heart sound is audible in most pregnant women, reflecting rapid ventricular filling. During the last trimester, increased mammary blood flow can produce a bruit that varies with the pressure of the stethoscope.

INVESTIGATIONS

Chest X-ray

The gestational increase in CO and pulmonary blood flow causes an increase in cardiothoracic ratio and pulmonary vascular markings. A chest X-ray is indicated in a pregnant woman who has new onset of dyspnoea. If the fetus is properly screened from X-rays the dose of radiation is less than 1 day of background radiation.

Electrocardiogram

The heart rate increases gradually throughout normal pregnancy to reach a mean of 88 beats per minute in the third trimester (Robson et al, 1989). As the diaphragm becomes elevated, the heart gradually changes position and the QRS axis moves to the left. Q waves and inverted T waves are frequently seen in lead III and aVR.

Echocardiography

Echocardiography is a safe and accurate method of discriminating significant heart disease from

Dr David Williams is Subspecialty Registrar in Maternal Medicine in the Institute of Obstetrics and Gynaecology, Queen Charlotte's Hospital, London W6 0XG

the physiological changes of healthy pregnancy. It is particularly useful when serially monitoring known valvular lesions throughout pregnancy. A degree of regurgitant flow across the tricuspid, mitral and pulmonary valves is a feature of of apparently normal pregnant women.

MATERNAL MORTALITY FROM HEART DISEASE

In the 9-year period from 1952 to 1960, following the beginning of the Confidential Enquiries into Maternal Deaths (CEMD) in the UK, heart disease caused about one-quarter of all indirect (i.e. not 'direct' obstetric) maternal deaths. This amounted to 42 maternal deaths from heart disease per million maternities. During this period the picture was dominated by rheumatic heart disease which caused 239 of the 277 cardiac deaths (*Figure 1*).

In the 9 years from 1985 to 1993 the death rate from heart disease represents about one-third of all indirect maternal deaths, but now this equates to just 11 deaths per million maternities (CEMD, 1996). The pattern of death from heart disease in the UK is now completely different from 1952 to 1960 (*Figure 1*). From 1985 to 1993, there were 50 deaths from acquired heart disease, of which 21 were ischaemic and 13 were the result of rupture of aneurysm of the thoracic aorta or its branches, and 28 deaths from congenital heart disease (CHD). Those dying from CHD included 11 (39%) with pulmonary vascular disease, who had either primary pulmonary hypertension (PPH) or Eisenmenger's complex.

SPECIFIC HEART DISEASES DURING PREGNANCY

Mitral stenosis

Mitral stenosis causes far more death and morbidity during pregnancy than any other rheumatic valve lesion. Breathlessness is the most common presenting symptom, which becomes worse during pregnancy because women with mitral stenosis have a limited ability to increase their CO. This is caused by the gestational increase in heart rate that reduces diastolic filling time through the stenotic mitral valve. The consequent rise in left atrial pressure, and gestational increase in pulmonary blood volume, makes these women particularly vulnerable to pulmonary oedema in the third trimester (de Swiet, 1995).

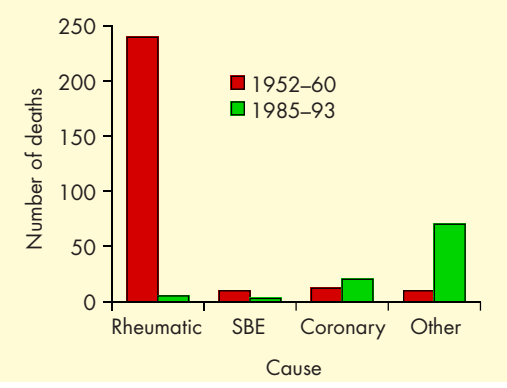

Figure 1. Deaths from heart disease 1952–60 and 1985–93. SBE = subacute bacterial endocarditis.

Furthermore, contraction of the uterus and relief of inferior vena cava compression immediately after delivery causes an increase in intravascular volume and a sharp rise in left atrial pressure, which can also result in acute pulmonary oedema (Clark et al, 1985). Patients who enter labour with a pulmonary artery wedge pressure of less than 14 mmHg are unlikely to develop pulmonary oedema (Clark et al, 1985).

The management of severe mitral stenosis should be aimed at improving left ventricular diastolic filling by slowing down the heart rate with β-blockers. Diuretics are necessary for the treatment of pulmonary oedema and cardioversion may be needed to treat atrial fibrillation (AF). Pregnant women with mitral stenosis and AF should be anticoagulated with warfarin, except during the first trimester and peripartum, when heparin prophylaxis will suffice (Ribeiro and Zaibag, 1997). If the clinical condition deteriorates despite medical treatment, then balloon or surgical valvotomy during pregnancy can give good results.

Mitral valve prolapse and regurgitation

Mitral valve prolapse and regurgitation are well tolerated during pregnancy. Systemic vasodilatation off-loads the left ventricle and the left atrial wall stretches which keeps left atrial pressure down. Women who have more than trivial mitral regurgitation require antibiotic prophylaxis.

Aortic stenosis and regurgitation

The severity of aortic stenosis can be over-estimated by echocardiography in pregnancy, because of increased flow across the valve. Conversely, a fall in stroke volume in patients with severe aortic stenosis causes a reduction in gradient. If the clinical condition deteriorates, then valve replacement may become necessary. Epidural anaesthesia causes peripheral vasodilatation and further increases the valvular gradient. The gestational fall in peripheral vascular resistance improves CO through a regurgitant aortic valve. Hence aortic regurgitation is usually well tolerated during pregnancy.

Infective endocarditis

The range of pathogenic organisms that can cause infective endocarditis during pregnancy

is similar to the non-pregnant state, although the urogenital tract is a common source of enterococcal endocarditis following obstetric surgical intervention (Lein and Stander, 1959). New heart murmurs are difficult to interpret during pregnancy as the gestational increase in blood flow intensifies murmurs from pre-existing heart lesions.

In one series, there were no cases of infective endocarditis following a normal delivery in over 2000 cardiac patients (Sugrue et al, 1980). Furthermore, although endocarditis was present in over 10% of cardiac deaths between 1985 and 1993 (CEMD, 1996), very rarely was it acquired at the time of delivery. However, CEMD included a women who died from bacterial endocarditis on a ventricular septal defect after a normal delivery. This shows that endocarditis can occur on heart lesions following normal delivery with catastrophic results.

Since it is difficult to predict if a delivery will remain 'uncomplicated', it is the authors' personal recommendation to give antibiotic prophylaxis to all women with structural heart lesions at the time of normal delivery. This is amoxycillin 1 g intramuscularly and gentamicin 120 mg intravenously (iv) at the time of induction of anaesthesia (or onset of labour), and then amoxycillin 500 mg orally (iv is preferable) 6 hours later (or every 6 hours while the patient is still in labour). Drugs are variably absorbed during labour, so oral amoxycillin 3 g to cover an anticipated normal delivery is best avoided.

ARTIFICIAL HEART VALVES AND ANTICOAGULATION

As the risk and consequences of valve thrombosis in pregnant women taking heparin exceeds the risks to the fetus of embryopathy, or haemorrhage when the mother takes warfarin (Oakley, 1997a). Therefore, young women needing valve replacement should have a mechanical valve and take warfarin throughout their pregnancy, except peripartum (see below), with a high expectation of successful fetal outcome.

However, warfarin crosses the placenta into the fetal circulation where it is a more potent anticoagulant. This is because of reduced production of vitamin K-dependent clotting factors by the fetal liver, rendering it at greater risk of haemorrhage throughout pregnancy and for up to 2 weeks after the mother stops warfarin. The quoted risk of fetal embryopathy (chondrodysplasia punctata) from taking warfarin in the first trimester is 3–4%, but this ignores the fact that warfarin-induced fetal embryopathy is dose dependent. In women taking less than 5 mg/day the risk of embryopathy is likely to be even less (Cottrufo et al, 1991). Women requiring higher doses of warfarin, especially over 10 mg, could protect their embryo by temporarily switching to iv heparin from the diagnosis of pregnancy, until the risk of embryopathy is over — approximately 12 weeks.

Delivery is best planned at 38 weeks gestation, warfarin should be stopped at least 1 week before delivery and therapeutic anticoagulation started with iv heparin infusion. This should continue until at least 1 week postpartum when warfarin can be restarted. Strategies that involve rapid reversal of anticoagulation by infusing fresh frozen plasma will correct maternal clotting, but as clotting factors do not pass into the fetal circulation, the fetus remains far more anticoagulated than the mother and at greater risk of haemorrhage. Warfarin does not pass into breast milk, so is safe for the breast-fed infant.

Heparin does not cross the placenta, but when given subcutaneously, it is less effective at preventing prosthetic valve thrombosis than warfarin. There are anecdotal cases of low molecular weight heparin successfully preventing mechanical valve thrombosis during pregnancy, but this strategy remains to be properly evaluated.

MYOCARDIAL INFARCTION

Myocardial infarction (MI) in pregnancy is often caused by coronary artery dissection (Kearney et al, 1993). Women present suddenly, without prodromal angina and usually in the third trimester or postpartum. The preponderance of arterial dissections associated with pregnancy may be related to increased haemodynamic shear stress on thin and dilated vessels.

The MB isoenzyme of creatinine phosphokinase is released from the myometrium postpartum, so other cardiac enzymes must be measured peripartum to diagnose a MI. If possible, immediate coronary angiography is indicated to discover the cause of the infarct. Both balloon angioplasty and coronary artery bypass grafting have been performed successfully during pregnancy. However, acute treatment with thrombolytic agents should not be delayed for coronary angiography if a large infarct is threatening the viability of the anterior wall.

The size of the infarct can be reduced by β-blockers given as soon as possible after the diagnosis. Although angiotensin-converting enzyme inhibitors cause oligohydramnios and reduce renal blood flow in the fetus, the benefits to a mother who has had a large infarct probably outweigh the risks to the fetus. Oxytocic drugs constrict coronary arteries as well as the uterus and

should be avoided. Ergotamine, used to prevent postpartum haemorrhage, can also provoke coronary artery spasm and has caused fatal MI in a previously healthy woman.

ARRHYTHMIAS

Women with non-ischaemic disease of cardiac conducting tissue, e.g. Wolff–Parkinson–White syndrome, have supraventricular tachycardias more frequently during pregnancy (Widerhorn et al, 1992). In general, antiarrhythmic drugs are safe in pregnancy and should be prescribed according to clinical need (Page, 1995). Most experience has been gained with digoxin, quinidine and β-adrenergic blocking drugs. Digoxin crosses the placenta to give similar drug levels in the fetus as in the mother, hence its use as a first-line treatment of fetal supraventricular arrhythmias in utero. Quinidine, procainamide and lignocaine are all well tolerated and relatively safe in pregnancy. Similarly, β-blockers are also well tolerated, especially in later pregnancy, but atenolol can cause intrauterine growth retardation when taken during the first half of pregnancy (Page, 1995). Amiodarone can cause fetal thyroid dysfunction and should be reserved for life-threatening arrhythmias. Verapamil has been widely used for the treatment of maternal supraventricular arrhythmias, but adenosine is now gaining favour, especially in the second and third trimesters.

Cardiac arrest in pregnancy

In late pregnancy, resuscitation in the supine position may fail as venous return and CO are compromised by aortocaval compression by the fetus. Turning the patient to relieve the compression can overcome this problem. If necessary cardioversion can be used without apparent harm to the fetus. If resuscitation is failing, emergency caesarean section may help maternal CO (Lee et al, 1986).

Peripartum cardiomyopathy

In the UK the incidence of peripartum cardiomyopathy is less than 1 in 5000 (de Swiet, 1995). Heart failure can develop peripartum (within 1 month of delivery and up to 6 months postpartum). However, women with multiple pregnancies are more likely to develop peripartum cardiomyopathy. Cases range from mild left ventricular dysfunction to sudden onset of gross heart failure and death within days of delivery. Arrhythmias are common and thrombus within a dilated left heart can embolize systemically at presentation.

An electrocardiogram will show sinus tachycardia, possibly with runs of supraventricular or ventricular arrhythmias. A chest X-ray can reveal a grossly dilated heart and pulmonary oedema. Echocardiography usually reveals dilatation of all four chambers of the heart and hypokinesia of the left ventricle.

The prognosis depends on the severity of the initial insult. While some women make a good recovery, others gradually decline to death or have a cardiac transplant. Four women had heart transplants following peripartum cardiomyopathy and all survived without any recurrence of their original heart disease. Even women who have made an apparently full recovery are likely to have lost some cardiac reserve in the initial insult. Therefore the haemodynamic challenge of a future pregnancy will always carry risks. Serial echocardiography to assess left ventricular function in a future pregnancy is sensible as the possibility of relapse remains.

Pulmonary hypertension

Whatever the aetiology, pulmonary hypertension is life threatening in pregnancy. PPH presents with dyspnoea and easy fatigability. The non-specific nature of these symptoms often means that the disease is not diagnosed until severe. Consequently, women who become pregnant with recognized PPH have severe disease and a maternal mortality of about 40% (Oakley, 1997b). An echocardiogram can exclude other cardiac disease, but may also reveal elevated pulmonary artery systolic pressure and a dominant right ventricle. As a result of the 40% maternal mortality and possibility of disease progression during pregnancy, any patient with PPH should be advised to have a termination. If the patient insists on continuing the pregnancy then maximum rest is advised because of the limited ability to increase CO and the possibility of right ventricular failure.

Management of PPH includes the use of vasodilators, such as calcium-channel blockers, that produce a sustained improvement in 25–30% of patients. Anticoagulation also has a place to prevent thrombosis in the pulmonary vasculature. Oxygen can provide symptomatic relief for hypoxic patients and diuretics have a place when right heart failure causes gross hepatic congestion and ascites. However, a high right filling pressure is required for maintenance of CO, therefore any fall in intravascular volume due to blood loss must be replaced promptly.

An elective caesarean section is preferable to vaginal delivery to prevent the physical exertion that will aggravate maternal and fetal hypoxia. A general anaesthetic is preferable to epidural anaesthesia, as the vasodilatation induced by the latter cannot be tolerated in patients with PPH and

a fixed CO. Postpartum management should take place on the intensive care unit with monitoring of the central venous pressure, systemic blood pressure and oxygen saturation. When death ensues, it is usually postpartum, precipitated by hypotension secondary to blood loss, arrhythmia, thromboembolism or right ventricular failure.

Cyanotic CHD

In general, women with cyanotic CHD, without Eisenmenger's complex (see below), can pass through pregnancy with low risk to themselves (Presbitero et al, 1994). However, maternal cardiovascular complications are frequent, and include heart failure, thromboses, bacterial endocarditis and supraventricular tachycardia. However, only 41 of 96 pregnancies resulted in a live birth, perhaps because of fetal hypoxaemia secondary to maternal cyanosis (Presbitero et al, 1994).

Eisenmenger's complex

The systemic vasodilatation of healthy pregnancy increases right–left blood flow through a septal defect. Consequently, cyanosis is make worse in pregnancy, and even minor blood loss can be fatal (Warnes, 1997). Women with Eisenmenger's complex who continue with a pregnancy have at least a 30% maternal mortality rate (Gleicher et al, 1975). They should be advised against pregnancy and to terminate an ongoing pregnancy. If continuation of pregnancy is insisted upon, they should have as much bed rest as possible and complete bed rest in the lateral position, from the third trimester onwards.

There is an increased risk of thromboembolism, which should be countered with subcutaneous heparin. There is no consensus regarding the mode of delivery, but either way, there should be intensive cardiac and blood gas monitoring. Hypotension must be avoided, whether induced by epidural anaesthesia, blood loss or arrhythmias. Most maternal deaths occur peripartum, therefore the mother must stay in hospital, near resuscitation facilities, until at least 14 days postpartum.

KEY POINTS

- Healthy pregnancy is a vasodilated state where cardiac output increases by 45%.
- Women with heart disease who cannot increase their cardiac output have the greatest morbidity.
- Primary pulmonary hypertension and Eisenmenger's complex are associated with a 30–50% mortality rate during pregnancy.
- The physiological changes of pregnancy aggravate the symptoms caused by aortic and mitral stenosis.

CONCLUSIONS

An understanding of the cardiovascular changes of healthy pregnancy is necessary to avoid misinterpreting the significance of new symptoms and signs. These changes are of little consequence to women with mitral valve prolapse, but can precipitate death in up to 50% of women with pulmonary hypertension. Knowledge of safe prescribing in pregnancy is essential to a successful pregnancy outcome for mother and infant. Women with CHD are now surviving to a fertile age and increasing numbers are becoming pregnant. All pregnant women with heart disease need to have access to centres that are expert in coordinating obstetric and cardiac care. HM

Clark SL, Phelan JP, Greenspoon J, Aldahl D, Monstein J (1985) Labour and delivery in the presence of mitral stenosis: central hemodynamic observations. *Am J Obstet Gynecol* **8:** 984–8

Confidential Enquiries into Maternal Deaths in the United Kingdom 1991–1993 (1996) *Confidential Enquiries into Maternal Deaths in the United Kingdom 1991–1993*. HMSO, London

Cottrufo M, de Luca TSL, Calabro R, Mastrogiovanni G, Lama D (1991) Coumarin anticoagulation during pregnancy in patients with mechanical heart valve prostheses. *Eur J Cardiothorac Surg* **5:** 300–5

De Swiet M (1995) Heart disease in pregnancy. In: De Swiet M, ed. *Medical Disorders in Obstetric Practice.* Blackwell Science Ltd, Oxford: 143–81

Gleicher N, Midwall J, Hochberger D, Jaffin H (1975) Eisenmenger's syndrome and pregnancy. *Obstet Gynecol Surv* **34:** 721–41

Kearney P, Singh H, Hutter J, Khan S, Lee G, Lucey J (1993) Spontaneous coronary artery dissection: a report of three cases and review of the literature. *Postgrad Med J* **69:** 940–5

Lee RV, Rodgers BD, White LM, Harvey RC (1986) Cardiopulmonary resuscitation of pregnant women. *Am J Med* **81:** 311–8

Lein JN, Stander RW (1959) Subacute bacterial endocarditis following obstetric and gynecologic procedures. *Obstet Gynecol* **13:** 568–73

Oakley CM (1997a) Artificial heart valves. In: Oakley CM ed. *Heart Disease in Pregnancy.* BMJ Publishing Group, London: 135–46

Oakley CM (1997b) Pulmonary hypertension. In: Oakley CM ed. *Heart Disease in Pregnancy.* BMJ Publishing Group, London: 97–111

Page RL (1995) Treatment of arrhythmias during pregnancy. *Am Heart J* **130:** 871–6

Presbitero P, Somerville J, Stone S, Aruta E, Spiegelhalter D, Rabajoli F (1994) Pregnancy in cyanotic congenital heart disease. Outcome of mother and fetus. *Circulation* **89:** 2673–6

Redman CWG (1995) Hypertension in pregnancy. In: De Swiet M ed. *Medical Disorders in Obstetric Practice*. Blackwell Science Ltd, Oxford: 182–225

Ribeiro P, Al Zaibag M (1997) Rheumatic heart disease. In: Oakley CM ed. *Heart Disease in Pregnancy.* BMJ Publishing Group, London: 112–27

Robson SC, Hunter S, Boys RJ, Dunlop W (1989) Serial study of factors influencing changes in cardiac output during human pregnancy. *Am J Physiol* **256:** H1060–5

Sugrue D, Blake S, Troy P, MacDonald D (1980) Antibiotic prophylaxis against infective endocarditis after normal delivery-is it necessary? *Br Heart J* **44:** 499–502

Warnes CA (1997) Cyanotic congenital heart disease. In: Oakley CM, ed. *Heart Disease in Pregnancy.* BMJ Publishing Group, London: 83–96

Widerhorn J, Widerhorn AL, Rahimtoola SH, Elkayam U (1992) WPW syndrome during pregnancy: increased incidence of supraventricular arrhythmias. *Am Heart J* **123:** 796–8