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SOCIETY OF
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Guidelines

Expert consensus document on management of cardiovascular diseases during pregnancy

The Task Force on the Management of Cardiovascular Diseases During Pregnancy of the European Society of Cardiology

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Preamble

Guidelines aim to present all the relevant evidence on a particular issue in order to help physicians to weigh the benefits and risks of a particular diagnostic or therapeutic procedure. They should be helpful in everyday clinical decision-making.

A great number of guidelines have been issued in recent years by different organisations—European Society of Cardiology (ESC), American Heart Association (AHA), American College of Cardiology (ACC), and other related societies. By means of links to web sites of National Societies several hundred guidelines are available. This profusion can put at stake the authority and validity of guidelines, which can only be guaranteed if they have been developed by an unquestionable decision-making process. This is one of the reasons why the ESC and others have issued recommendations for formulating and issuing guidelines, which are quoted as a preamble or appendix in the final reports.

In spite of the fact that standards for issuing good quality guidelines are well defined, recent surveys of guidelines published in peer-reviewed

journals between 1985 and 1998 have shown that methodological standards were not complied within the vast majority of cases. It is therefore of great importance that guidelines and recommendations are presented in formats that are easily interpreted. Subsequently, their implementation programmes must also be well conducted. Attempts have been made to determine whether guidelines improve the quality of clinical practice and the utilisation of health resources. In addition, the legal implications of medical guidelines have been discussed and examined, resulting in position documents, which have been published by a specific Task Force.

The *ESC Committee for Practice Guidelines and Policy Conferences (CPGPC)* supervises and coordinates the preparation of new *Guidelines* and *Expert Consensus Documents* produced by Task Forces, expert groups or consensus panels. The Committee is also responsible for the endorsement of these guidelines or statements.

This document defines the procedure and rules for developing and issuing guidelines and expert consensus documents, from the moment of conception of the Task Force or expert group to the final publication of the document.

Introduction

This document is addressed to cardiologists whose young and not so young female patients may desire pregnancy, seek advice once pregnant or in whom heart disease is first discovered during pregnancy.

The focus is on those conditions which threaten the life or health of mother or baby with only short mention of those that are well tolerated. We emphasise the haemodynamic principles on which determination of likely outcomes are based, stressing the importance of early consultation where there is doubt and of team work between all those concerned: physicians, cardiologists, general practitioners, obstetricians, anaesthetists and geneticists as appropriate.

Management of cardiac diseases during pregnancy

Most women with heart disease have successful pregnancies but most cardiologists and obstetricians see only small numbers. Pregnant women seek local care but women with known or suspected heart disease, unexplained shortness of breath or other symptoms in pregnancy or planning pregnancy should be referred to a specialist centre. Experienced cardiologists working as a team with

obstetricians, anaesthetists, clinical geneticists and neonatologists will advise. Shared care can then be organised with the local hospital and GP with the extent of surveillance, site and mode of delivery arranged according to individual need.

The success of neonatal surgery has greatly increased survival and allowed infants with complex congenital anomalies to reach adulthood. Women with congenital heart disease now far outnumber those with rheumatic heart disease in pregnancy except in developing countries. Because rheumatic valve disease is now rare in the West except in immigrants, it can sometimes be missed and shortness of breath wrongly ascribed to the pregnancy itself or to asthma rather than to mitral stenosis or pulmonary hypertension. Modern echo along with an ECG usually provides all the means needed for completing the clinical diagnosis. Chest X-rays should be restricted during pregnancy and shield protection used but they can provide valuable information not otherwise easily obtained. The likely response to the haemodynamic changes in pregnancy can then be assessed but if heart disease is not even considered the patient will never get as far as an echo study or a cardiologist.

Most, but importantly not all, patients with heart disease in NYHA classes I and II will have a successful outcome. Some conditions, like mitral or aortic stenosis, can give trouble even when symptoms were absent or no problem was even realised to exist before the pregnancy. The dangerous conditions are: pulmonary vascular disease (whatever its cause), fragile aortas as in Marfan syndrome, left sided obstructions and already dilated poorly functioning left ventricles. The risk is obviously high in any woman in NYHA class III or IV.

Women with pre-existing disease are less able to cope with superimposed conditions acquired in pregnancy such as peripartum cardiomyopathy (PPCM) and are more at risk from complications such as pulmonary embolism, arrhythmias and stroke. These and spontaneous dissection of a coronary artery (or indeed the aorta) can smite the previously healthy though they are rare.

Cardiologists rely more on evidence from randomised trials than any other speciality in medicine but there is no such evidence base from which to guide management in pregnancy. Both clinicians and patients would probably be reluctant to join such trials and recruitment of adequate numbers would be difficult.

Drugs prescribed in pregnancy have crept into common use without trial and their use continued as long as their track record remains good. Oral anticoagulants are the exception as they remain in

use for patients with mechanical valves but only because there is no equally effective alternative.

Management is guided by observational studies and these have been consistent in linking risk to functional class^{1,2} and emphasising the dangers faced by women with pulmonary vascular disease.^{3,4} A recent multi-centre study from Canada reported on 562 women referred between 1994 and 1999 but did not describe large enough numbers of individual condition for statistical validity. Heart disease was congenital in three quarters of the Canadian women (none of whom had severe pulmonary hypertension or the Eisenmenger syndrome) and acquired in only a fifth.⁵ The study reinforced the existing body of knowledge of risks in pregnancy and emphasised the differences in case mix between the West and the developing world. Mitral stenosis is still a major cause of death related to pregnancy in these countries in which the greatest experience in both closed and balloon mitral valvotomy has been acquired.

Haemodynamic modifications during pregnancy

Hormonal changes, which relax smooth muscle, followed by formation of the placenta and foetal circulation, determine an increase in blood volume which starts to rise as early as the fifth week. The increase reaches 50% towards the end of pregnancy and is greater in multiple pregnancies than singletons. Both systemic vascular resistance and blood pressure decrease and the resting heart rate increases by 10–20 beats per minute. The result is an increase of 30–50% in cardiac output, which is mainly achieved by an increase in stroke volume.⁶ Failure to achieve this is marked by a resting tachycardia which provides evidence of diminished cardiovascular reserve and which is itself detrimental in conditions in which left ventricular filling is slow.

Labour and delivery feature a further increase in cardiac output and also in blood pressure particularly during uterine contractions and an increase in oxygen consumption. These haemodynamic modifications are heavily influenced by the mode of delivery.⁷

Cardiac output is also increased during the early postpartum period because additional blood reaches the circulation from the contracting uterus determining an increase in preload.⁸ That is why at-risk patients often develop pulmonary oedema at this stage. Haemodynamic conditions have largely returned to normal within 1–3 days in most cases but may take up to a week.

Congenital heart disease

Haemodynamic changes during pregnancy can exacerbate the problems associated with congenital heart disease.⁶ The outcome is related to functional class (NYHA classification), the nature of the disease and previous cardiac surgery.

High-risk patients

Any patient who reaches functional class III or IV during pregnancy is at high risk whatever the underlying condition as this means that there is no remaining cardiovascular reserve. The situations carrying highest risk are as follows.

Pulmonary hypertension

Severe pulmonary vascular disease whether with (in the Eisenmenger syndrome) or without septal defects has long been known to carry the highest risk (maternal mortality 30–50%).^{4,9} This is mainly because of a life-threatening further rise in pulmonary vascular resistance due to pulmonary thrombosis or fibrinoid necrosis which develops particularly fast in the peripartum and postpartum periods and can determine a fatal outcome even in patients who previously had little or no disability. In the Eisenmenger syndrome right to left shunting increases during pregnancy because of systemic vasodilatation and right ventricular overload with increased cyanosis and decrease in pulmonary blood flow.

Severe left ventricular outflow tract obstruction

A fixed outflow tract resistance may not be able to accommodate the increased cardiac output caused by increased plasma volume. This can lead to heart failure with a detrimental rise in left ventricular and pulmonary capillary pressures, low output and pulmonary congestion.¹⁰

Cyanotic heart disease

The over all maternal mortality is around 2% with high risk of complications (30%) such as infective endocarditis, arrhythmias and congestive heart failure (CHF).¹¹ The foetal prognosis is also very poor with a high risk of spontaneous abortion (50%), premature delivery (30–50%) and low-for-dates birth weight because maternal hypoxaemia impairs foetal growth.

Thromboembolism is one of the risks in high-risk pregnancies and the use of prophylactic heparin should be considered especially after surgical delivery and in the puerperium.

Treatment of high-risk patients

Pregnancy is not recommended. If pregnancy occurs, termination should be advised as the risks to the mother are high (mortality 8–35%, morbidity 50%). Even termination of pregnancy has its attendant risks because of vasodilatation and depression of myocardial contractility due to anaesthesia.

Physical activity should be restricted and bed rest is recommended if symptoms occur. Oxygen should be given if hypoxaemia is evident. The patient should be hospitalised by the end of the second trimester and low molecular weight heparin administered subcutaneously, as prophylaxis against thromboembolism particularly in cyanotic patients.

In severe aortic stenosis, it is especially important to monitor systemic pressure and the ECG, as changes can indicate the appearance or worsening of left ventricular overload. Balloon valvotomy can relieve symptomatic and severe cases if the valve is pliable. This procedure is best performed in the second trimester when embryogenesis is complete and to avoid any negative effect of ionic contrast agents on the foetal thyroid late in gestation. The radiation dose to the abdomen of the mother is low, between 0.05 and 0.2 rads.¹² Ballooning is contraindicated if the valve is calcified or there is already significant regurgitation. Surgery is the alternative. Cardiopulmonary by-pass has a foetal mortality of 20%¹³ so every effort should be made to continue the pregnancy until the foetus is viable and to deliver the baby by caesarean section before the cardiac surgery.

In severe cyanotic heart disease, monitoring of oxygen saturation is very important. Haematocrit and haemoglobin levels are not reliable indicators of hypoxaemia due to the haemodilution that occurs in pregnancy. If severe hypoxaemia is present and termination of pregnancy is refused some kind of shunt should be implanted if feasible to improve oxygenation.

Low risk patients

Patients with small or moderate shunts without pulmonary hypertension or mild or moderate valve regurgitation benefit from the decrease of systemic vascular resistance that occurs during pregnancy. Patients with mild or moderate left ventricular outflow tract obstruction also tolerate pregnancy well.¹⁰ In such cases the pressure gradient increases steadily as the stroke output rises. Even moderately severe right ventricular outflow tract obstruction (pulmonary stenosis) is well tolerated

and only rarely needs intervention during pregnancy.

Most patients who have had cardiac surgery early in life without prosthetic valves can tolerate pregnancy well. However, residual defects are present in 2–50% of cases and need to be assessed clinically as well as with echocardiography. In these low risk cases it is reasonable to reassure the patients and follow them with a cardiac assessment every trimester. Assessment of congenital heart disease in the foetus should be done by foetal echocardiography.

Specific conditions

Pulmonary valve stenosis

Right ventricular outflow tract (RVOT) obstruction tends to be well tolerated during pregnancy despite the gestational volume overload imposed on an already pressure-loaded right ventricle. No deaths and a low incidence of minor maternal complications (about 15%) have been reported. When the stenosis is severe pregnancy may precipitate right heart failure, atrial arrhythmias, or tricuspid regurgitation, irrespective of the presence of symptoms prior to pregnancy. Patients with severe RVOT obstruction should, therefore, be considered for its relief prior to conception. In cases of right ventricular failure during pregnancy, balloon valvulotomy is the option of choice for severe valve stenosis (four cases have been reported with no complications).¹⁴

Tetralogy of Fallot

Pregnancy in unoperated patients carries a risk of maternal and foetal complications, which is tied to the degree of maternal cyanosis. The risk is high when oxygen saturation is <85%.¹¹ The rise in blood volume and venous return to the right atrium with a fall in systemic vascular resistance increases the right to left shunt and cyanosis. Close monitoring of systemic blood pressure and blood gases during labour is needed and any further systemic vasodilatation (drug induced) avoided.

The risk of pregnancy in repaired patients depends on their haemodynamic status. The risk is low, approaching that of the general population, in patients with good repairs. In patients with significant residual RVOT obstruction, severe pulmonary regurgitation with or without tricuspid regurgitation and/or RV dysfunction, the increased volume load of pregnancy may lead to right heart failure and arrhythmias. All patients with tetralogy should have genetic counselling pre-conception with assessment in case of 22q11 deletion syndrome using fluorescent in situ hybridisation (FISH). In its absence the risk of defects in the foetus is low (about 4%).¹⁵

Coarctation of the aorta

Coarctation of the aorta should be repaired prior to pregnancy. It is rare during pregnancy (9% of all congenital defects). The management of hypertension is difficult in the unoperated pregnant patient. Foetal growth is usually normal and in contrast to essential hypertension pre-eclamptic toxemia does not occur but over enthusiastic treatment may cause too low a pressure in the distal segment. This may result in abortion or foetal death even though pressure in the proximal segment continues to rise on effort. Rupture of the aorta is the commonest reported cause of death¹⁶ and rupture of an aneurysm of the circle of Willis has also been reported during pregnancy. The increase in blood volume and cardiac output increases the risk of aortic dissection or rupture during pregnancy and a beta-blocker should be prescribed.

Restriction of physical activity is the only way of minimising potentially dangerous surges in blood pressure. Surgical correction is only very rarely indicated during pregnancy if systolic hypertension is uncontrolled or heart failure is present. Balloon angioplasty is contra-indicated because of the risk of dissection or rupture. Whether this risk is avoidable with stenting is not known.

Intra-atrial repair for transposition of great arteries (TGA)

Over 100 pregnancies have been reported in the literature with no deaths. In women in functional class I–II pregnancy is usually well tolerated. Worsening of systemic ventricular function during or shortly after pregnancy occurred in 10% of the reported cases.¹⁷ ACE inhibitors should be stopped before pregnancy or as soon as possible. Frequent review is recommended.

Congenitally corrected transposition of the great arteries

Women without significant other cardiac defects usually do well but problems can develop through failure of the systemic right ventricle with increasing regurgitation through its tricuspid atrioventricular valve. Supraventricular arrhythmias, embolism and atrioventricular block are other potential complications.¹⁸

Fontan procedure

Pregnancy carries additional risk to the mother because of the increased haemodynamic burden on the right atrium and the single ventricle. A maternal death rate of 2% is reported.¹⁹ Increase in venous congestion and deterioration in ventricular function are the most common complications. Atrial arrhythmias tend to develop or worsen. Right atrial thrombus formation may occur with a risk of paradoxical embolism if the Fontan is fenestrated.

Spontaneous abortion is frequent and occurs in up to 40% of the cases, probably because of congestion of the intra-uterine veins. Only 45% of live births at term have been reported. Careful patient selection is important. The successful Fontan with a small right atrium or total cavopulmonary connection (TCPC) in functional class II or I can probably complete pregnancy with a normal live birth. Fontan patients with a large right atrium and some venous congestion have to be monitored very carefully. They need anticoagulant treatment and conversion to TCPC before pregnancy is considered.

Arrhythmias in pregnancy associated with congenital heart disease (see also Section 11)

The incidence of arrhythmias, both ventricular and supra ventricular, increases during pregnancy due to haemodynamic, hormonal and emotional changes.²⁰ In most congenital heart diseases right atrial and/or ventricular pressure or volume increase and arrhythmias, particularly supra-ventricular arrhythmias, occur in 10–60% of cases. During pregnancy arrhythmias become even more frequent and develop in up to 80% of patients. Physiological changes in pregnancy may alter the absorption and excretion and effective plasma concentration of all antiarrhythmic drugs.²¹

When chronic antiarrhythmic treatment is needed to prevent episodes of arrhythmia digoxin is usually the first drug prescribed but it is ineffective. Quinidine, verapamil and beta-blockers have been used for long-term treatment of supraventricular and ventricular arrhythmias in both mother and foetus without any evidence of teratogenic effects.²¹ Amiodarone is a potent antiarrhythmic but should be used only when other therapy has failed and then at the lowest effective dose.²² All these drugs have a depressive effect on myocardial contractility so they have to be used with caution in the presence of an impaired left or right ventricle.

Episodes of sustained tachycardia (particularly atrial flutter which is the most common arrhythmia in adult congenital heart disease) that are not well tolerated can cause foetal hypo-perfusion and emergency DC conversion should be performed to restore sinus rhythm. If the tachycardia is haemodynamically well tolerated, drug therapy should be attempted.

Foetal assessment

In every pregnant woman with congenital heart disease foetal cardiac assessment is necessary because there is a 2–16% risk of congenital heart disease in the foetus.¹⁵ The incidence of congenital heart disease in the offspring is more common

Table 1 Pregnancy and congenital heart disease incidence of CHD in offspring

Total 4.10%	Mother 5.00%	Father 2.00%
Fallot	2.5%	1.5%
LV obstruction	10–18%	3.00%
VSD	6.00%	2.00%
ASD	4.50%	1.50%

in the foetus when the mother rather than the father is affected particularly if the mother has a condition like bicuspid aortic valve which is more common in the male (See Table 1).

In a population at specific risk the detection rate of congenital heart disease is high (75–85%). Affected foetuses benefit from delivery in a tertiary care centre, but the main importance of an early (before 24 weeks of gestation) diagnosis is the possibility of termination of the pregnancy (TOP). The two main determinants of foetal prognosis are maternal functional class and the degree of maternal cyanosis. When the mother is in functional class III–IV, or in high-risk diseases such as severe aortic stenosis, Eisenmenger syndrome, etc early delivery is usually a good option. It will be obligatory in cyanosed women in whom monitoring of foetal growth is very important because it usually slows up and ceases before term. The survival rate for pre-term neonates is high after 32 weeks (95%) and the risk of neurological sequelae is low so if the pregnancy is ≥ 32 weeks delivery should be expedited. Since the survival rate is low before 28 weeks (<75%) and the risk of brain damage in the surviving neonates is high (10–14%) surgery or percutaneous procedures should if feasible be undertaken in order to postpone delivery as long as possible.

The choice may be difficult between 28 and 32 weeks, and decisions must be individualised. If the foetus is going to be delivered at ≤ 34 weeks, lung maturation must be induced by betamethasone administration to the mother.

Timing and mode of delivery

In the majority of patients, spontaneous delivery is indicated using epidural anaesthesia in order to avoid the stress of pain during delivery. In high-risk patients, elective caesarean section should be performed. This allows the haemodynamics to be kept more stable. Although the cardiac output increases during both general and epidural anaesthesia the increase is less (30%) than during spontaneous delivery (50%).^{7,23} Moreover, induction of labour at an early gestational age often fails or takes a long

time. If heart surgery is needed caesarean section can be performed immediately before it. Haemodynamic parameters and blood gases should be monitored during delivery. In patients with congenital heart disease in pregnancy, a multidisciplinary approach in consultation with cardiologists, cardiac surgeons, anaesthesiologists, obstetricians, neonatologists and geneticists is needed to minimise the risk to both mother and child.

Marfan syndrome and other inherited conditions affecting the aorta

Of the major inherited disorders affecting the heart and aorta during pregnancy, Marfan syndrome, with a population incidence of 1 in 5000, is the most important worldwide. Eleven types of Ehlers–Danlos syndrome have now been characterised, with a combined incidence of 1 in 5000 births. Aortic involvement is seen primarily in Ehlers–Danlos syndrome type IV. Other familial forms of thoracic aortic aneurysm and dissection also present problems of management in pregnancy.

Marfan syndrome

Marfan syndrome is the most serious dominantly inherited fibrillin-1 deficiency disorder, affecting all systems, but mainly eyes, heart and skeleton. Signs of classical involvement in two out of three main systems constitute the clinical diagnostic criteria.²⁴ In 25% of patients the syndrome results from a spontaneous mutation, but in 75% of cases there is a family history of other affected relatives. The pregnancy history of affected females, and, if available, their aortic root diameter at the time of dissection or aortic root surgery is helpful in deciding a plan of management. The ages at which aortic aneurysms occur in other females is an approximate guide but there is great clinical variability even within a family.

Maternal health

Eighty percent of Marfan patients have some cardiac involvement.²⁵ The majority have mitral valve prolapse with mitral regurgitation and possibly associated arrhythmia. Mitral valve repair may be necessary before pregnancy.

Aortic aneurysm, rupture and dissection are still the commonest causes of death in Marfan syndrome. Pregnancy is a high-risk period for affected females, with dissection occurring most often in the last trimester or the early postpartum period.²⁶ Full assessment should be performed before preg-

nancy and include ultrasound examination of the heart and entire aorta. Women with minimal cardiac involvement (aortic root diameter less than 4.0 cm, and no significant aortic or mitral regurgitation) should be informed of a 1% risk of aortic dissection or other serious cardiac complication such as endocarditis or congestive cardiac failure during pregnancy.²⁷ Patients with an aortic root diameter of more than 4 cm should be told that the risk of dissection during pregnancy is 10%.^{28,29} The pros and cons of pregnancy should be fully discussed as well as the alternatives (childlessness, adoption, surrogate pregnancy).²⁶

The risk is lower for pregnancy following elective aortic root replacement for aortic root diameters of 4.7 cm and over. A number of patients have successfully undergone elective aortic root replacement, and subsequently had successful full term pregnancies without complication. One patient went on to have a second successful pregnancy but following this developed an aneurysm of the aortic arch which has since been successfully replaced. These patients need to be monitored by echocardiography of the remaining aorta at 6–8 week intervals throughout the pregnancy and for 6 months postpartum. Betablocker therapy should be continued throughout the pregnancy. Each pregnancy should be supervised by a cardiologist and obstetrician who are alert to the possible complications.

Delivery

If normal delivery is planned the second stage should be expedited. The woman may be allowed to labour on her left side or in a semi-erect position to minimise stress on the aorta. If the aortic root diameter is 4.5 cm or greater caesarean delivery is advised.

Aortic dissection during pregnancy

Acute dissection of the ascending aorta is a surgical emergency.³⁰ Repair with a composite graft is the procedure of choice.³¹ Preservation of the aortic valve³² or its replacement with a homograft avoids the need for long-term anticoagulants. Normothermic bypass, progesterone per vaginum and continuous foetal heart monitoring reduce the risk to the foetus. Poor wound healing is a feature of Marfan syndrome, as is postpartum haemorrhage and an increased tendency to prolapse of pelvic organs. Sutures should be left in longer than normal and antibiotic cover extended until the sutures are removed.

Acute dissection with origin beyond the left subclavian artery and not involving the proximal aorta should be managed medically. This does not usually

need surgery and can be followed by serial MRI. Progressive dilatation to 5 cm or more, recurrent pain, or signs consistent with fresh dissection such as the development of organ or limb ischaemia, are all indications for repair.³³ The baby, if viable, should be delivered by caesarean section before going on to bypass.

The anaesthetic management of caesarean section followed by repair of aortic dissection should minimise foetal exposure to depressant drugs while ensuring a well-controlled haemodynamic environment for the mother.³³ Epidural and spinal anaesthesia should be undertaken only after consideration of the possibility of dural ectasia as arachnoid cysts could result in considerable dilution.³⁴

Health of the newborn

Babies with Marfan syndrome tend to be long and thin with wise-looking faces, high palate and long fingers. They may be hypotonic and have difficulty feeding. Ophthalmological examination for lens dislocation should be performed soon after birth.

Genetic testing

Almost 200 mutations have been reported in the fibrillin-1 gene, and almost every patient has a unique mutation. At present, if a mutation has been identified in an affected parent, diagnosis can be made by chorionic villus biopsy at 13 weeks gestation, by amniocentesis cell culture or postnatally using cord blood, or buccal rub sample from the infant. If parents simply wish to know whether the infant is affected, testing should be offered in the newborn period. This avoids the 1% risk of miscarriage incurred during foetal sampling.

Ehlers–Danlos syndrome

This heterogeneous group of inherited connective tissue disorders is characterised by articular hypermobility, skin hyperextensibility, and tissue fragility. Together they occur in 1 in 5000 births. Aortic involvement occurs almost exclusively in EDS type IV³⁵ which is transmitted as an autosomal dominant. Affected women are usually of short, slim build with prematurely aged hands, triangular faces, large eyes and small chins, thin pinched noses and small lobeless ears. During pregnancy, women may show increased bruising, hernias, varicosities, or suffer rupture of large blood vessels.³⁶ Aortic dissection may occur without dilatation. The course of pregnancy and delivery should be closely monitored. Postpartum haemorrhage may be severe. Incisions heal slowly and it is suggested that retention sutures be used, and not removed

for at least 14 days, to avoid wound dehiscence. Prematurity and precipitous deliveries are common because of lax cervical connective tissue, and weak membranes. Affected infants tend to be hyperextensible and may have congenitally dislocated hips. Floppiness and bleeding tendency may also be features.

Familial thoracic aortic aneurysms and dissections

Some patients have a family history of aortic dissection in the absence of overt Marfan syndrome.³⁷ Close examination of affected surviving family members may indicate Marfanoid habitus to a minor degree. Frequently the surgical histopathology of the aorta indicates cystic medial necrosis, as in Marfan syndrome. Some patients demonstrate mutations in the fibrillin-1 gene³⁸ and recently, two other gene loci have been identified in such families.

Pregnancy in such patients should be managed in an identical fashion to that in Marfan syndrome patients.

Summary

Joint cardiac and obstetric management of high-risk pregnancies in women with inherited tendency to aortic aneurysm and dissection should include regular echocardiograms before, during and after pregnancy. Hypertension and arrhythmia should be closely controlled. Aortic surgery during pregnancy bears a high risk of foetal mortality. It may be avoided through elective aortic root replacement with preservation of valve or a homograft, prior to pregnancy. Caesarean section should be reserved for those with aortic roots over 4.5 cm, or delayed second stage. Betablocker therapy should be continued throughout pregnancy. Postpartum haemorrhage can be expected. The newborn should have careful physical, echocardiographic and ophthalmic examination. Alternatives to pregnancy should be discussed with high-risk patients.

Acquired valvular heart disease

Rheumatic heart valve disease remains a major problem for public health in developing countries. In western countries, even though the prevalence of rheumatic fever has declined considerably, rheumatic heart diseases are still seen. This is particularly the case in immigrants who have not had optimal access to health care facilities. Besides native heart valve diseases, specific problems are encountered in women with heart valve prostheses

during pregnancy, mainly related to anticoagulant therapy.

Regurgitant valve disease

Severe mitral or aortic regurgitation in young women is frequently of rheumatic origin. Severe dystrophic regurgitation is seldom encountered in young women in the absence of Marfan syndrome or previous infective endocarditis.³⁹ The prognosis of pregnancy in women with mitral valve prolapse is excellent unless the regurgitation is severe and poorly tolerated.⁴⁰

The increase in blood volume and cardiac output will increase the volume overload consequent upon the valvular regurgitation but the decrease in systemic vascular resistance reduces the regurgitant fraction which compensates in part for this. In aortic regurgitation the shortening of diastole consequent on tachycardia also contributes to a reduction in the regurgitant volume. This explains why pregnancy is frequently well tolerated even in patients with severe valve regurgitation. Haemodynamic tolerance is worse in the rare cases of acute regurgitation because of the absence of left ventricular dilatation.⁴¹

Patients may develop progressive CHF, particularly during the third trimester. They need diuretics plus vasodilators to reduce after-load even further unless blood pressure is low.⁴² Angiotensin receptor antagonists and ACE inhibitors are contra-indicated and since the withdrawal of hydralazine from use during the first and second trimesters of pregnancy the only available vasodilators are nitrates and the dihydropyridine calcium-channel blockers. Vaginal delivery may be carried out safely in most patients, even those who have experienced transient heart failure, using the same medication. Haemodynamic monitoring is needed only in the severest cases.

Surgery should be avoided during pregnancy because of the risk to the foetus and considered only in patients with refractory heart failure, which is very infrequent in valvular regurgitation.⁴³ Repair of the mitral valve is preferable whenever possible but preservation of the aortic valve is rarely successful (except in Marfan syndrome).

Stenotic heart valve disease

An increase in cardiac output across the stenosed valve will determine a sharp increase in the transvalvular gradient and pregnancy may be

poorly tolerated in patients with severe mitral or aortic valve stenosis. The onset of functional worsening occurs most frequently during the second trimester.⁴⁴

Mitral stenosis

Mitral stenosis is the most frequently encountered valve disease in pregnant women and it is nearly always of rheumatic origin.^{2,44} The transmitral gradient increases particularly during the second and third trimester and tachycardia by shortening diastole contributes to a further rise in left atrial pressure.⁴⁵ In patients with a mitral valve area $<1.5 \text{ cm}^2$ (or $1 \text{ cm}^2/\text{m}^2$ of body surface area) pregnancy carries a risk of pulmonary oedema, CHF, arrhythmia and intra-uterine growth retardation.⁴⁴

Close follow-up is necessary in every pregnant woman with severe mitral stenosis, even if she was totally asymptomatic before pregnancy or during the first trimester.^{44,46} The mean transmitral gradient and pulmonary artery pressure should be measured by Doppler echocardiography at three and five months and monthly thereafter.

Medical treatment with beta blockers^{46,47} should be started in patients who have symptoms or estimated systolic pulmonary artery pressure $>50 \text{ mmHg}$. Choice of selective agents such as atenolol or metoprolol limits the risk of interaction with uterine contractions.⁴⁸ Adjustment of the dosage should take into account mean gradient, pulmonary artery pressure and functional tolerance. High doses are frequently required by the end of pregnancy. Diuretics need to be added if signs of pulmonary congestion persist. If the patient still has symptoms and/or pulmonary hypertension despite medical therapy there is a high risk of pulmonary oedema at delivery or during the postpartum period, threatening the life of both mother and foetus⁴⁹⁻⁵¹ and relief of the mitral stenosis is indicated.

The risk of foetal death during open-heart surgery is estimated to lie between 20 and 30% and is unpredictable^{13,52-56} but short of death, signs of distress have been documented by foetal monitoring during cardiopulmonary bypass.^{57,58} For this reason, closed mitral valvotomy has been considered the procedure of choice during pregnancy.⁵⁹ It is safe for the mother but carries a foetal mortality of between 2 and 12%, even in series published in the eighties.⁶⁰⁻⁶³

Percutaneous balloon mitral valvotomy (PMV) has now replaced surgery. Its feasibility and safety during pregnancy are well established. Published series now total more than 250 patients.⁶⁴⁻⁷⁷ Haemodynamic results are good because young

Table 2 Frequency of foetal and maternal complications according to the anticoagulation regimen used during pregnancy in women with mechanical heart valve prosthesis. Adapted from Chan et al.⁵¹

Anticoagulation regimen	Embryopathy (%)	Spontaneous abortion (%)	Thromboembolic complications (%)	Maternal death (%)
Vitamin K antagonists throughout pregnancy ^a	6.4	25	3.9	1.8
Heparin throughout pregnancy	0	24	33	15
Low dose	0	20	60	40
Adjusted dose	0	25	25	6.7
Heparin during first trimester, then vitamin K antagonists ^a	3.4	25	9.2	4.2

^aWith or without heparin prior to delivery.

women usually have favourable anatomy. Functional status improves and pregnancy continues until vaginal delivery of a healthy newborn. Radiation exposure is minimised by shielding the abdomen and omitting haemodynamic measurement and angiography. The ease of use of the Inoue balloon is of particular importance in keeping the procedure as short as possible.

Foetal safety has been demonstrated by periprocedural foetal monitoring and measurement of radiation exposure.⁶⁸ There is a 5% risk of severe traumatic mitral regurgitation, which is generally poorly tolerated and requires emergency surgery under cardiopulmonary bypass. This is particularly dangerous for the foetus.^{70,72} The risk of tamponade or embolic events during PMV is very low.

Because of these potential complications PMV should only be performed in highly experienced centres¹² and limited to pregnant patients who remain symptomatic despite medical therapy.⁷⁸ It is not recommended prophylactically or in patients who have severe mitral stenosis but no pulmonary hypertension and good functional tolerance. The same is true for closed mitral valvotomy, which for economic reasons remains the most frequent intervention for mitral stenosis in developing countries. In rare cases PMV needs to be performed in emergency as a lifesaving procedure in critically ill pregnant patients.⁷⁸

Aortic stenosis

Severe aortic stenosis is far less frequent than mitral stenosis in pregnancy. Most cases are congenital, less frequently, rheumatic when it is usually associated with mitral stenosis. Delivery is safe in patients whose functional tolerance is good.⁷⁹

In rare cases where patients remain severely symptomatic, in particular if they have signs of heart failure, aortic stenosis should be relieved before delivery. Percutaneous balloon aortic

valvotomy should be attempted when possible to avoid aortic valve replacement^{12, 80–83} but is risky during pregnancy and should only be considered in experienced centres in very selected cases.

Pregnancy in women with heart valve prostheses

The haemodynamic tolerance of pregnancy and delivery is generally good in women who have undergone heart valve replacement. The problem is the need for anticoagulant therapy in patients with mechanical prostheses which can be summarised as follows:

1. a hypercoagulable state exists throughout pregnancy⁸⁴ and
2. vitamin K antagonists cross the placenta and increase the risk of early abortion, embryopathy and prematurity.

The incidence of embryopathy is still debated. The overall risk seems to be around 5% in patients who receive vitamin K antagonists between the sixth and the twelfth weeks,⁸⁵ although lower rates have been reported⁸⁶ and the risk is dose related. Vitamin K antagonists should be withdrawn before delivery.⁸⁷ Unfractionated heparin does not cross the placenta but long-term heparin therapy during pregnancy is difficult to manage and considerably increases the thromboembolic risk for the mother.⁸⁵

There are no randomised trials allowing for an accurate comparison of different anticoagulation regimens during pregnancy. A recent review of the literature reported a total of 1234 pregnancies in 976 women with mechanical heart valve prostheses, two-thirds of which were in the mitral position (Table 2).⁸⁵ It indicated that the use of heparin throughout pregnancy leads to a prohibitive incidence of thromboembolic events, even when using adjusted doses. There is agreement to the use of vitamin K antagonists during the second and third

trimester of pregnancy. The usual recommendation is that they should be replaced by percutaneous or intravenous heparin at the 36th week to avoid the risk of neonatal intracranial haemorrhage during delivery.⁸⁷ The alternative is elective caesarean section at 36 weeks. This is frequently needed in any case because labour often begins prematurely while the foetus is still anticoagulated and it is sensible because it minimises the period on heparin.

There is no consensus regarding treatment during the first trimester.^{88–93} The continuation of vitamin K antagonists allows safe and stable anticoagulation for the mother. Recent data suggest that the risk of abortion or embryopathy is very low in patients who take ≤ 5 mg of warfarin per day.⁹⁴ The alternative is to use subcutaneous unfractionated heparin during the first trimester, particularly between the sixth and twelfth week. This regimen decreases the risk of embryopathy to zero only if heparin is started before the sixth week.⁸⁵ However, in addition to the discomfort and the risks of thrombocytopenia and osteoporosis subcutaneous heparin during the first trimester is associated with a high incidence of thromboembolic complications particularly prosthetic thrombosis. Consistent data show that continuation of vitamin K antagonists during the first trimester is the safest therapeutic option for the mother.^{85,86,95–98}

The choice should be made after clearly informing the patient and her partner of the risks inherent in the different anticoagulation modalities. Potential medico-legal concerns should also be considered as the label states that warfarin is contra-indicated during pregnancy. The target INR is the same and the dose does not usually change.

Low-molecular weight heparin has advantages over unfractionated heparin, notably, it provides a more stable anticoagulation level.⁹⁹ Its efficacy has been demonstrated during pregnancy in venous thromboembolism¹⁰⁰ but it has been used in only a small number of pregnant women with heart valve prostheses.^{99,101,102} The safety and efficacy of such treatment has not been documented in patients with mechanical heart valves outside pregnancy. Although its use is mentioned in recent recommendations,¹⁰³ our opinion is that low-molecular weight heparin should not be recommended at the present time in patients with heart valve prostheses during pregnancy. Whatever the anticoagulation regimen, pregnancy in a patient with a mechanical prosthesis is associated with a maternal mortality between 1 and 4%, mainly due to valve thrombosis while on heparin therapy.

Valve repair before conception should be performed whenever possible or biological substitutes considered. Although pregnancy per se may not accelerate bioprosthesis degeneration¹⁰⁴ durability is still poor in young adults and patients need to accept the inevitability of re-operation in a few years time while their children are still young¹⁰⁵ and to understand that it carries risk.

Mode of delivery

Despite greater haemodynamic stress vaginal delivery under epidural analgesia is safe in patients with heart valve disease provided they are in stable condition.⁴⁴ Obstetrical procedures to shorten the total duration of labour particularly the second stage may be helpful.¹⁰⁶ Invasive haemodynamic monitoring is indicated only in patients with severe valve stenosis or recent heart failure.^{49,107}

Caesarean section has the advantage of avoiding the physical stress of labour, but it is not free from haemodynamic consequences related to anaesthesia and assisted ventilation and the increased risk of venous thromboembolism needs to be countered.

In all cases the modality of delivery should be discussed between cardiologists, obstetricians, anaesthetists and the patient. It is preferable to set the date so that the whole medical team can be ready.

In patients on anticoagulant therapy, heparin should be withdrawn 4 h before caesarean section or at the onset of labour and resumed 6–12 h after either surgical or vaginal delivery.

In high-risk patients with previous endocarditis or heart valve prostheses, prophylactic antibiotic treatment should be given at the beginning of labour and during delivery.

Breast-feeding can be encouraged in women taking anticoagulants. Heparin is not secreted in breast milk and the amount of warfarin is low.¹⁰⁸

Recommendations

- Echocardiographic evaluation should be performed in any young woman who has valvular heart disease, even in the absence of symptoms.
- The management of the valve disease should, whenever possible, be discussed before the onset of pregnancy, particularly in cases of mitral stenosis $< 1.5 \text{ cm}^2$ suitable for percutaneous mitral valvotomy and in cases of aortic stenosis $< 1.0 \text{ cm}^2$.
- Close follow-up is mandatory after the beginning of the second trimester.

- In cases of poor functional tolerance, medical treatment should include beta-blockers in severe mitral stenosis, vasodilators in regurgitant valve disease and diuretics.
- Percutaneous mitral valvotomy is indicated during pregnancy only if the patient remains symptomatic despite medical therapy.
- Open heart surgery should be performed only when the mother's life is threatened and if viable the foetus should be delivered beforehand.
- In a pregnant patient with a mechanical prosthesis, the choice of anticoagulant therapy during the first trimester should take into account the greater thromboembolic risk with heparin and the risk of embryopathy with vitamin K antagonists. The use of vitamin K antagonists during the first trimester is the safest regimen for the mother.
- Delivery should if possible be planned and its modality discussed in close collaboration with the obstetricians and anaesthetists.

Coronary artery disease

Atheromatous coronary artery disease is uncommon in pregnancy but not as rare as it was. Apart from familial hypercholesterolaemia, smoking, obesity and diabetes as well as older age at conception account for increasing numbers. Such women may develop angina during pregnancy and need treatment to provide them with sufficient coronary flow reserve to carry them safely through the pregnancy. Exercise testing is important in assessing this. If beta-blockers and calcium antagonists are insufficient percutaneous intervention (PCI) can be performed with care to minimise the radiation dose to the foetus. The second trimester is the best time to do this. Patients with already known coronary disease should of course be assessed and treated before conceiving. Previous coronary bypass surgery is not a contraindication if the woman is fit. The genetic consequences of having a child who will be an obligate heterozygote need to be discussed in women with homozygous or combined heterozygotic hypercholesterolaemia. These patients also develop left ventricular outflow obstruction due to a narrowed aortic root combined with immobilisation of the aortic valve cusps by xanthomatous deposits in the aortic sinuses. If determined on pregnancy they should embark on it early.

Sudden severe chest pain in a previously fit pregnant woman may be caused by dissection of the

aorta. If the pain is caused by myocardial infarction it is most likely that spontaneous dissection of a coronary artery has occurred.¹⁰⁹ Thrombolytics should therefore not be given (they are only relatively contra-indicated in pregnancy) but immediate coronary angiography performed with a view to PCI with stenting. Dissection can occur in any or more than one coronary artery and the indication for intervention depends on the site and apparent size of the evolving infarct.

Congenital coronary anomalies are also encountered occasionally. Coronary-cameral and coronary pulmonary artery fistulae do not usually cause any problem. Coronary arteritis due to previous Kawasaki Disease with aneurysm formation and thrombosis (which may be new) may present with angina or infarction in pregnancy and need coronary grafting. This should preferably not be done on bypass but it may be unavoidable. Coronary arteritis may also be associated with on-going autoimmune vascular disease and present with infarction in pregnancy or the puerperium.^{110,111}

Coronary angiography is essential for recognition of the mechanism and anatomy of the infarct to enable management of it to be appropriate. Most tend to occur in the peripartum period and need differentiation from PPCM if heart failure has occurred.

Cardiomyopathies

Peripartum cardiomyopathy

This is a form of dilated cardiomyopathy (DCM) that occurs in the peripartum period in previously healthy women. It is defined as unexplained left ventricular systolic dysfunction confirmed echocardiographically which develops in the last month prenatally or within five months of delivery.¹¹² This definition is intended to exclude pre-existing DCM¹¹³ which may have been present but unsuspected before the pregnancy as DCM is likely to be exacerbated by the pregnancy and to present before the last month. There are few accounts of DCM in pregnancy probably because overt cases are discouraged from becoming pregnant. Case reports usually describe marked deterioration.

Women who have developed a PPCM usually present with heart failure with marked fluid retention, less often with embolic stroke or arrhythmia. The worst cases tend to develop during the first few days postpartum. Failure may be fulminating and require inotropes, a ventricular assist device or even transplantation. As ventricular function

usually (but not always) eventually improves, implantation of a device is much preferable to transplantation if they can be got through the worst period. As in acute myocarditis outside pregnancy the most fulminant cases show the most capacity to improve (as well as to die) and in them the use of a device as a bridge to recovery is particularly appropriate.

Less severe cases require standard therapy for heart failure and their left ventricular function followed carefully. Anticoagulants are important as the risk of systemic embolism is high. Improvement may be delayed but continue for a year or more but in some cases function deteriorates and transplantation is then appropriate. A survey of 44 women with a history of PPCM who had a total of 60 subsequent pregnancies showed a high relapse rate in subsequent pregnancies.¹¹⁴ This was not confined to women with residual left ventricular dilatation. It was seen also among women whose function had apparently returned to normal but there were no fatalities in this group. Other experience has been more encouraging¹¹⁵ but reported numbers are small.

Cardiac biopsy usually shows acute myocarditis if it is performed early after onset. The cause is unknown but possibly an immune reaction to the 'foreign' foetus. Immunosuppressive therapy may therefore be appropriate but there are only observational data to support this. Immune globulin has also been tried with apparent benefit in a small number of women.¹¹⁶

The most frequent time of presentation is during the first few days postpartum. Haemodynamic stress should be abating except that this is a period of hypervolaemia in those women who have suffered little blood loss during delivery. Hyperhydration may be a factor after operative delivery with which PPCM is particularly associated. However, when PPCM in milder form is first seen later in the puerperium it can only be blamed on the pregnancy itself or on the unlikely and coincidental development of DCM at this time. PPCM also sometimes affects women with pre-existing heart disease and diminished cardiovascular reserve but whose left ventricular function had previously been documented to be normal.^{117,118}

Dilated cardiomyopathy

It is only very rarely that DCM is well documented before the pregnancy. In most cases pregnancy is avoided on medical advice and patients with dilated left ventricles are only occasionally first diagnosed in early or mid gestation. If symptoms first

develop in the last month of pregnancy the title "peripartum" is given with the question concerning previous left ventricular function unanswered and unanswerable.

If there is a family history of DCM this may be a clue to pre-existing but occult dysfunction in a patient who develops first symptoms within the artificial time envelope necessarily assigned the designation "peripartum". The often explosive early postpartum onset or later, quieter, presentation at a time of no haemodynamic load is so distinctive that PPCM deserves its separate category.

Patients with DCM should be advised against pregnancy because of the high chance of deterioration both during gestation and peripartum. If pregnancy occurs, termination should be advised if the ejection fraction is <50% and/or the LV dimensions are definitely above normal.

If termination is refused the patient must be seen frequently and LV function checked by echo. Early admission to hospital is wise especially as both ACE inhibitors and angiotensin II antagonists are contra-indicated and treatment options are much more limited than outside pregnancy.

Recommendations

- Echocardiography should be performed, before conception if possible, in all patients in whom DCM is known or suspected or who has a family history of DCM or of PPCM.
- Pregnancy should be discouraged if left ventricular contractile function is reduced because of a high risk of deterioration.
- In patients with a family history of DCM a greater risk of PPCM should be given consideration.
- Pregnant patients with DCM are at high risk and should be admitted to hospital if there is any evidence of deterioration.

Hypertrophic cardiomyopathy

Women with hypertrophic cardiomyopathy usually tolerate pregnancy well as the left ventricle seems to adapt in a physiological way.¹¹⁹ This is especially advantageous in this condition in which the cavity dimensions tend to be small. Fatalities have been reported during pregnancy but are rare. A case report of systolic dysfunction developing postpartum may well have been PPCM.¹²⁰

Women with a murmur and outflow tract gradient are especially likely to be first diagnosed in pregnancy. Considerable distress may be caused by

the diagnosis and by the genetic implications. This is not helped by the considerable publicity given in the lay press to the risk of sudden death. In the absence of a family history of sudden death asymptomatic patients can be told that their risks are low and that pregnancy is usually completed successfully. After the diagnostic echo and an ECG, exercise testing and ambulatory ECG monitoring and genetic counselling are carried out as in the non-pregnant patient.

Women with severe diastolic dysfunction can cause concern with pulmonary congestion or even sudden pulmonary oedema. This may develop on exertion or emotion but is most likely to occur peripartum. Beta-blockers should be continued and a small dose of diuretic may help but rest in conjunction with the beta-blocker to prevent tachycardia is essential in these rare high-risk patients. It is wise to give low dose heparin.

If atrial fibrillation (AF) develops anticoagulation is imperative. Low molecular weight heparin is suitable. If new onset AF fails to revert to sinus rhythm, DC reversion may be necessary after excluding left atrial thrombus by transoesophageal echo. A beta-blocker will help control the ventricular rate in AF and to prevent recurrence. Digoxin is not contra-indicated as these patients rarely have outflow gradients.

Patients with persistent arrhythmias, particularly symptomatic ventricular arrhythmias, which have developed during pregnancy, may need amiodarone despite the risk of inducing foetal hypothyroidism. It is particularly effective in conjunction with a beta-blocker.

Normal delivery on a selected date should be conducted with continuation of a beta-blocker and avoidance of systemic vasodilatation. Any blood loss should be replaced but care should be taken not to cause fluid overload in high-risk patients with very labile left atrial pressures.

The genetic risk needs to be discussed including the phenomenon of anticipation, which determines an earlier onset and more severe form in succeeding generations in some families.

Recommendations

- Most asymptomatic patients with HCM do well.
- Medication should be confined to treatment of symptoms.
- Patients with severe diastolic dysfunction will need rest and medication in hospital.
- Pulmonary congestion or oedema are most likely to occur in the third stage, delivery should always be in hospital and the date planned.

Infective endocarditis

Infective endocarditis is rare in pregnancy but can present some difficult problems in management. The increase in blood volume and output can precipitate failure caused by fever and worsening structural damage. Antibiotics must be chosen to save the life of the mother but also to try to avoid damage to the foetus. The need for surgical treatment must be weighed against the risk of losing the infant but should not be delayed if the indication is acute valvar regurgitation or conduit or shunt obstruction nor if the organism is a virulent staphylococcus in a non-responding toxic patient. In such cases the temptation to delay surgery until after delivery should be resisted. If the baby is viable it should be delivered before the cardiac surgery.

Prophylactic antibiotics

The indications for antibiotic prophylaxis are the same as in the non-pregnant state to cover dental or other procedures or conditions likely to cause Gram positive bacteraemia.

The incidence of bacteraemia following normal delivery is between 0 and 5%.^{121,122} Moreover the bacteraemia when it occurs is low grade and may be due to many different organisms. The risk of infective endocarditis complicating normal delivery is extremely low.¹²³ Nevertheless prophylaxis is indicated in patients with prosthetic valves or previous endocarditis and may be chosen in other patients with anticipated normal delivery because complications are unpredictable. Antibiotics should of course be given before surgical delivery or cardiac surgery.

Recommendations

- Diagnosis and treatment are the same as outside pregnancy.
- If gentamicin has to be used its levels need to be checked with particular care because of the risk of causing foetal deafness.
- Decisions for surgery should be made early as the foetal risk is dependent on the maternal condition.
- Antibiotic prophylaxis is discretionary for normal delivery but should be given to patients with prosthetic valves or a history of previous endocarditis.

Arrhythmias

Both ectopic beats and sustained arrhythmias become more frequent during pregnancy when they

may even develop for the first time.²⁰ In general they are treated in the same way as outside pregnancy but as conservatively as possible reserving definitive treatment for later if it is safe to do so.¹¹⁶

All commonly used antiarrhythmic drugs cross the placenta. The pharmacokinetics of drugs are altered in pregnancy and blood levels need to be checked to ensure maximum efficacy and avoid toxicity.

Patients worried about ectopic beats can usually be reassured unless the frequency increases on exercise. Supraventricular tachycardias are corrected by vagal stimulation or, failing that, intravenous adenosine. Electrical cardioversion is not contra-indicated and should be used for any sustained tachycardia causing haemodynamic instability and therefore threatening foetal security. Beta blocking drugs with beta-1 selectivity are the first choice for prophylaxis. Verapamil is constipating, many patients do not feel well on sotalol and verapamil and though they may be effective they tend to cause foetal bradycardia. Radio frequency ablation for AV nodal re-entry or certain AV re-entry tachycardias can if necessary be performed during pregnancy with suitable lead shielding and maximal use of echo rather than X-ray fluoroscopy.

If a class 1C agent is needed amiodarone is preferable to sotalol. Lesser amounts of amiodarone cross the placenta (the foetal concentration is only 20% of maternal concentration), it has a less depressant effect on ventricular function than other agents and has little pro-arrhythmic or lethal risk compared with other antiarrhythmic drugs. Long-term use can cause neonatal hypothyroidism (9% of newborns), hyperthyroidism and goitre, so it should only be used when other therapy has failed and the arrhythmia causes haemodynamic instability with risk of foetal hypoperfusion.²²

Potentially life threatening ventricular tachyarrhythmias are much less common and should be terminated by electrical cardioversion. Beta-1 selective beta-blockers alone, amiodarone alone or the combination, may be effective in prevention but if ineffective an ICD will be needed. The presence of an ICD does not itself contra-indicate future pregnancy.¹¹⁷

A pacemaker for the alleviation of symptomatic bradycardia can be implanted at any stage of pregnancy using echo guidance.

Hypertensive disorders

Hypertension is the most commonly occurring complication of pregnancy. Hypertensive disorders have remained one of the leading causes of both

maternal and perinatal morbidity and mortality. Management has not changed significantly for many years because of little progress in our understanding and lack of an evidence base for the introduction of new therapies.

Classification and definitions¹¹⁸

- Chronic hypertension, pre-existing hypertension +/- proteinuria in a patient with pre-existing disease diagnosed prior to, during or after pregnancy.
- Pre-eclampsia–eclampsia. Proteinuria (>300 mg over 24 h or ++ in two urine samples) in addition to new hypertension. Oedema is no longer included in the diagnosis of pre-eclampsia because of its poor specificity.
- Pre-eclampsia superimposed on chronic hypertension. Increased blood pressure above the patient's baseline, a change in proteinuria or evidence of end-organ dysfunction.
- Gestational hypertension. New hypertension with a blood pressure of 140/90 on two separate occasions, arising de novo after the 20th week of pregnancy.

Korotkoff V is now recommended for the measurement of diastolic blood pressure in pregnancy as it corresponds most closely to the intra-arterial pressure.^{118,119}

In women with pre-existing hypertension raised blood pressure is the main feature. By contrast, in the more ominous condition of pre-eclampsia, raised blood pressure is one sign of a syndrome resulting from an underlying systemic endothelial disorder with vasospasm, reduced organ perfusion and activation of the coagulation cascade.

It is believed that pre-eclampsia is caused by placental hypoperfusion due to failure of remodelling (dilatation) of the maternal spiral arteries and release of a (still unknown) circulating factor which causes changes in systemic endothelial function. The HELLP syndrome is defined by haemolysis, elevated liver enzymes and low platelets. Headache, visual disturbance and pulmonary oedema may also occur.¹²⁰

Superimposed pre-eclampsia develops in 20–25% of women with chronic hypertension and carries risk to both mother and baby.

Gestational hypertension is distinguished from pre-eclampsia by lack of proteinuria and is termed transient hypertension of pregnancy if the blood pressure has returned to normal by 12 weeks postpartum and as chronic hypertension if it is still raised. Gestational hypertension mandates close

attention as about half will develop pre-eclampsia¹²¹ and if symptoms or abnormal haematological or biochemical markers are found pre-eclampsia is likely even if proteinuria is absent.¹¹⁹

Chronic hypertension is present before the 20th week of gestation whereas the pregnancy specific condition of pre-eclampsia is rarely seen before 20 weeks except in the presence of trophoblast diseases such as hydatidiform mole.

Chronic hypertension

Maternal complications of hypertension include abruptio placentae and cerebral haemorrhage as well as superimposed pre-eclampsia. Foetal complications include prematurity and dysmaturity, still-birth and neonatal death.

Management of low-risk hypertension

Control of hypertension should begin before conception. Low risk patients have essential hypertension with BP between 140–160/90–110, normal physical examination, normal ECG and echo and no proteinuria. Several studies have shown that antihypertensive drugs are effective in preventing exacerbation of high blood pressure in pregnancy^{122,123} but antihypertensive treatment has not been shown to be effective in preventing superimposed pre-eclampsia nor is perinatal mortality affected regardless of the drugs used. Only a few randomised trials have been performed. None of the drugs tested had adverse effects on outcome. Atenolol has been associated with an increased incidence of small for dates babies and a lower placental weight but there was no difference at 1 year.¹²⁴

As in non-hypertensives the blood pressure tends to fall during pregnancy so it may be possible to discontinue drug treatment. Frequent supervision is essential because the patient may become high risk through development of severe hypertension or pre-eclampsia. Drug treatment will be needed for maternal protection if the BP rises but provided foetal growth is normal the pregnancy can continue until term. Hospital admission or delivery will be indicated if pre-eclampsia develops or foetal growth slows.

High-risk patients

Conditions associated with micro-vascular disease can affect placentation and carry an increased risk of pre-eclampsia. Maternal and foetal genotypes also contribute.¹²⁵ High-risk patients have severe

hypertension with evidence of end-organ involvement, a poor obstetric history or co-morbidity from renal impairment, diabetes or collagen vascular disease.¹²⁵ These women need individual assessment, counselling and frequent assessment of blood and urine chemistry and of foetal growth.

For ethical reasons there are no placebo controlled trials of pharmacological regimes for the treatment of severe hypertension in pregnancy. Both maternal and foetal mortality used to be high in severe hypertensives largely because of superimposed pre-eclamptic toxemia whose mortality has since been reduced by anticipation and early recognition rather than by effective treatment. Antihypertensive therapy is indicated for the mother and may also benefit the foetus by securing prolongation of the pregnancy.

Pharmacological treatment

- Methyl dopa remains the first line agent because it has the best safety record with no evidence of adverse effects in mothers or babies including long term paediatric follow-up. The dose is 750 mg to 4 g per day in three or four divided doses.¹²⁶
- Beta blocking drugs have had extensive use. The alpha beta-blocker, labetalol has the advantage of vasodilatation. The dose is 100 mg twice daily up to 2400 mg per day. None of the beta-blockers have been associated with teratogenicity. When given only late in pregnancy atenolol, metoprolol, pindolol and oxprenolol have not been associated with any adverse effects. Like atenolol labetalol has been linked to low weight for gestational age but no such association was found in one large trial in which labetalol was started at between 6 and 13 weeks gestation.¹²⁴
- Calcium channel blockers, mainly nifedipine, have not been found either beneficial or detrimental¹²⁷ but if given sublingually or intravenously rapid and excessive BP reduction has caused myocardial infarction or foetal distress. Myocardial depression may follow combination of a calcium blocker with intravenous magnesium.¹²⁸
- Clonidine has been used mainly in the third trimester without report of adverse outcome. The usual dose is 0.1–0.3 mg per day in divided doses up to 1.2 mg per day.¹²³
- The use of diuretics is controversial because they reduce plasma volume expansion so causing concern that their use might promote the occurrence of pre-eclampsia. Although there is

no evidence of this diuretics should only be used in combination with other drugs particularly when vasodilators exacerbate fluid retention as they markedly potentiate the response to other antihypertensive agents. Diuretics are contra-indicated as utero-placental circulation perfusion is already reduced in pre-eclampsia with foetal growth retardation (remembering that the changes in vascular reactivity and plasma volume antedate even by weeks the clinical features of pre-eclampsia¹²⁹). If needed a thiazide should be chosen. Frusemide has been used safely in pregnancy complicated by renal or cardiac failure.

Pregnant women with renal disease are usually hypertensive. Foetal survival is markedly reduced and birth weight decreases with increases in creatinine. Volume overload may increase and reduce drug responsiveness requiring salt restriction, loop diuretics or dialysis. Increasing proteinuria masks pre-eclampsia. Low birth weight and premature delivery are the rule.

- ACE inhibitors are contra-indicated during the second and third trimesters because they cause renal dysgenesis.¹³⁰
- Hydralazine has been widely used to control severe pre-eclampsia and no adverse effects followed its use for chronic hypertension in the second and third trimesters but it was found to be inferior to other agents.¹²⁰

Management of post partum hypertension

Resolution of hypertension may be delayed and renal failure, encephalopathy and pulmonary oedema may develop during the postpartum period particularly in patients with chronic renal or cardiac disease and superimposed pre-eclampsia. This reflects the time needed for endothelial repair. Gestational hypertension usually resolves quickly. Breast-feeding is to be encouraged. Although most antihypertensive agents are excreted in milk there are few data on any effects on the neonate. Atenolol, metoprolol and nadolol are concentrated in breast milk and diuretics reduce milk volume so these agents should be avoided in nursing mothers.¹³¹

Pre-eclampsia

Lack of knowledge of its cause precludes prevention of pre-eclampsia. Identification and early diagnosis of women at high risk permits close monitoring and carefully timed delivery.

Pre-eclampsia is completely reversible and usually begins to abate with delivery which is always appropriate treatment for the mother but not for the foetus in whom maturation is the main aim. The key question is always whether the foetus is more likely to survive in utero or in the nursery.

The aim is to reduce maternal vascular complications without critically reducing utero-placental blood flow and thereby exacerbating the condition. Restriction of activity is usual. Randomised trials have shown no improvement in foetal outcome from antihypertensive therapy.^{122,127}

Treatment of acute hypertension

The most commonly used parenteral therapies are nifedipine, labetalol and hydralazine.

The use of magnesium sulphate for severe pre-eclampsia and eclampsia is now well established though little is understood about its mode of action. Treatment with antihypertensive drugs and magnesium sulphate in hospital may be followed by some improvement and such management may prolong pregnancy and decrease perinatal mortality and morbidity. Close maternal and foetal surveillance are essential as prompt delivery is indicated by worsening of the maternal condition, laboratory evidence of end-organ dysfunction or foetal distress. Delivery is the only definitive treatment for pre-eclampsia.

Steroids should be given for 48 h to accelerate lung maturation if gestation is <34 weeks.

- The use of low molecular weight heparin in patients with a known coagulopathy or previous history of pre-eclampsia remains controversial.
- Aspirin
A recent Cochrane review showed a 15% reduction in the incidence of pre-eclampsia and a 7% fall in deliveries before 37 weeks but little overall improvement in foetal outcome and the data are conflicting.^{132,133}
- Antioxidants
If free radicals promote endothelial dysfunction antioxidants might help. Endothelial function can be improved in vitro by ascorbic acid but a randomised trial of vitamins C and E showed no difference in perinatal outcome.¹³⁴

Summary

Pregnant women with hypertension are at risk. Careful management has reduced maternal and foetal complications. Drug treatment does not improve perinatal outcome in women at low risk but

antihypertensive treatment should be used to protect women with high-risk hypertension. Although understanding of pre-eclampsia has advanced there is still no specific treatment for it. Therapeutic strategies are aimed at ameliorating the maternal response but the only intervention available to improve perinatal outcome is timely delivery.

Summary

- *Women at low risk in pregnancy* are those who have few or no symptoms and good ventricular function without haemodynamically compromising or potentially life threatening arrhythmias. They lack severe left ventricular inflow or outflow obstruction, do not have significant pulmonary or systemic hypertension and do not need to take anticoagulants.
- After full cardiac assessment, low risk patients can be managed locally while maintaining potential links with the obstetric cardiac centre should any question or problem arise.
- *Patients at higher risk* need to be managed within or from the cardiac centre and the highest risk patients will need admission from about 20 weeks.
- *The mode and time of delivery* should be discussed and decisions made well in advance. Vaginal delivery is usually advised. Exceptions are patients with dilated Marfan aortic roots or aortic dissections, uncorrected coarctation, pulmonary vascular disease (including Eisenmenger syndrome) and/or cyanosis and patients with mechanical valve prostheses in order to minimise the period of heparin withdrawal. Epidural anaesthesia is favoured but vasodilatation should be avoided in patients with cyanosis or when stroke output is compromised. Adequate fluid volume loading is important but should not be overdone in patients with left ventricular obstruction or severe hypertrophic cardiomyopathy. Invasive monitoring is rarely justified by its inherent risks.
- *Antibiotic prophylaxis* is discretionary for anticipated normal delivery. The risk of endocarditis has been shown to be very low and the benefits have not been proved but cover is logical and wise for surgical deliveries, for patients with intracardiac prostheses of any sort and for patients who have had previous endocarditis.
- *In patients with pulmonary hypertension* postpartum monitoring should continue for up to a week and be conducted in the CCU for high-risk patients with continuous pulse oximetry as this is their period of highest risk when an increase

in pulmonary vascular resistance needs to be combated most aggressively.

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