

# Pregnancy and contraception in heart disease and pulmonary arterial hypertension

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## Introduction

Heart disease is the leading cause of maternal mortality in the UK.<sup>1</sup> There is therefore a need to disseminate amongst the medical profession accurate information about contraception and pre-pregnancy counselling for women with heart disease.

The risk of pregnancy depends on the specific disease and the individual patient. For example, the risk of maternal death is up to 50% for those with pulmonary arterial hypertension, but there is no anticipated extra risk for those with mild pulmonary stenosis compared to women without heart disease. Similarly, although certain contraceptive methods are associated with unacceptable increases in risk for specific cardiac conditions, it is not the case that "most structural heart disease" is an absolute contraindication for use of the combined oral contraceptive (COC).<sup>2</sup>

There is a paucity of published information and very little evidence base about contraception in women with heart disease. Thus health care professionals who offer advice to such women may err on the side of caution, being reluctant to advise some methods that may in fact be appropriate. A lack of knowledge by non-specialists of the

range of effective contraceptive measures available may result in the highest-risk women being denied effective contraception and having unplanned pregnancies.<sup>3</sup> Conversely, those with less severe lesions receive inappropriate advice regarding (primarily) oral contraception, again leading to unintended conceptions.<sup>3</sup> In extreme examples, women may even be advised to undergo unnecessary termination of pregnancy for a cardiac condition that has little or no increased risk in pregnancy.

The lack of specialist cardiac services for the growing number of adolescents and adults with congenital heart disease (CHD) may compound the problem. Many cardiologists have little knowledge of the interactions between complex heart disease, pregnancy and its prevention. Family planning needs and preconceptual advice for adults with CHD are presently generally poorly provided for.<sup>3</sup> All these women need advice arising from a combined approach between family planning clinicians and cardiologists with relevant special skills and interests. This counselling should always respect the woman's autonomy.

For the above reasons, a group of obstetricians, gynaecologists, experts in contraception, obstetric physicians, cardiologists and specialists in adult CHD was convened. This working group met on several occasions and corresponded over 2 years to produce a consensus document outlining recommendations on pregnancy and contraception for women with heart disease. Since women with heart disease are not a homogeneous group, the aim of this review and the resulting recommendations is to provide risk stratification for both pregnancy and individual contraceptive methods in women with cardiac disease.

**Table 1** World Health Organization (WHO) risk classifications by medical condition for contraceptive method and pregnancy

| WHO Class | Risk for contraceptive method by medical condition   | Risk for pregnancy by medical condition   |
|-----------|--|---|
| 1         | Condition with no restriction for the use of the contraceptive method<br>Always usable   | No detectable increased risk of maternal mortality or morbidity   |
| 2         | Condition where the advantages of the method generally outweigh the risks<br>Broadly usable  | Small increased risk of maternal mortality or morbidity   |
| 3         | Condition where the risks of the method usually outweigh the advantages: alternatives are usually preferable. Exceptions if:<br>(i) Patient accepts risks and rejects alternatives<br>(ii) The risk of pregnancy is very high and the only acceptable alternative methods are less effective<br>Caution in use | Significantly increased risk of maternal mortality or severe morbidity. Expert counselling required. If pregnancy is decided upon, intensive specialist cardiac and obstetric monitoring needed throughout pregnancy, childbirth and the puerperium |
| 4         | Condition where the method represents an unacceptable health risk<br>Do not use  | Extremely high risk of maternal mortality or severe morbidity: pregnancy contraindicated. If pregnancy occurs termination should be discussed. If pregnancy continues, care as for Class 3  |

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The working group agreed that the World Health Organization (WHO) classification of contraindications for contraceptive use would be a useful tool for addressing suitability of specific contraceptive methods<sup>4,5</sup> and, in addition, could be modified to stratify risk for pregnancy in heart disease (Table 1).

Discussion of the risks of pregnancy and reasons for advising a particular contraceptive method must be documented in the patient's notes. This is particularly relevant to WHO Classes 3 and 4.

### Risks of pregnancy

All women with heart disease should be referred to, or discussed with, a cardiologist with relevant skills prior to conceiving. For those with CHD, discussions regarding pregnancy and contraception should be initiated in the paediatric cardiology clinics as part of the broader process of transition to adulthood.

All women with CHD should have access to preconception counselling from a specialist in adult CHD.

This section classifies maternal risk according to cardiac condition. Risk is additive, so for each individual, the risk of a pregnancy may move up a class if there are further risk factors such as hypertension, diabetes and major musculoskeletal abnormalities.

The risk of an adverse cardiac event during the pregnancy of a woman with heart disease may also be estimated from the following risk factors:

- cyanosis ( $\text{SaO}_2 < 90\%$ )
- New York Heart Association (NYHA) symptoms >Functional Class II
- systemic ventricular ejection fraction <40%
- prior cardiovascular event (arrhythmia, pulmonary oedema, stroke or transient ischaemic attack).

If one risk factor is present, the additional risk of an adverse cardiac event in the current pregnancy is 27%; if two or more, the risk is 75%.<sup>6</sup>

### Class 4 Conditions (Table 2)

- Pregnancy presents an extremely high risk of maternal mortality or severe morbidity and is contraindicated. If pregnancy occurs, termination should be discussed. If pregnancy continues, care as for Class 3.

#### Pulmonary arterial hypertension

Pulmonary arterial hypertension<sup>7,8</sup> from any cause is associated with a maternal mortality of up to 50%.<sup>9</sup> It is believed that it is the increase in pulmonary vascular resistance with subsequent inability to increase pulmonary blood flow that makes pregnancy so dangerous and places it in the Class 4 category.

Pulmonary arterial hypertension is defined as a non-pregnant elevation of *mean* (not systolic) pulmonary artery pressure  $\geq 25$  mmHg at rest or 30 mmHg on exercise in the absence of a left-to-right shunt. Mild pulmonary arterial hypertension can also be defined as a pulmonary artery *systolic* pressure of ~36–50 mmHg.

Pulmonary artery systolic pressure is usually estimated by using Doppler ultrasound to measure the regurgitant jet velocity across the tricuspid valve. A peak tricuspid

regurgitant velocity of 2.8–3.4 m/s (assuming a normal right atrial pressure of 5 mmHg) equates to mild pulmonary hypertension. It should be noted that the pulmonary artery pressure falls in the presence of moderate to severe right ventricular impairment, thus underestimating the severity of pulmonary vascular disease. A Doppler estimate of pulmonary artery systolic pressure should be considered a screening test and a specialist cardiac opinion sought if pulmonary hypertension is suspected.

The risk of maternal death is high even in the presence of mild pulmonary hypertension. Furthermore, recent UK maternal mortality data suggest that pregnancy can be associated with progression of pulmonary hypertension.<sup>1</sup>

#### Significant left heart obstruction

Significant left heart obstruction as defined by echocardiography:

Mitral stenosis: mitral valve area <1.0 cm<sup>2</sup>

Aortic stenosis: aortic valve area <1.0 cm<sup>2</sup> or (non-pregnant) *mean* gradient >50 mmHg.

Lower aortic valve pressure differences may be falsely reassuring: if left ventricular systolic function is impaired, the left ventricle may not be capable of generating a high gradient across the aortic valve. In addition, if the patient is symptomatic, has a blood pressure which fails to rise normally in response to exercise, marked ST segment changes or impaired left ventricular function, then pregnancy can be very high risk, whatever the estimated Doppler gradient.

It should be remembered that the increased cardiac output of pregnancy increases the Doppler flow velocity and hence the estimated gradient across the aortic valve. Failure of the aortic valve gradient to rise during pregnancy may therefore indicate a failing left ventricle.

#### Marfan syndrome

Type A aortic dissection is the main maternal risk in Marfan syndrome; it carries a 22% mortality in pregnancy.<sup>10</sup> The overall risk of maternal death is approximately 1%. Women at particularly high risk include those with a poor family history, cardiac involvement and aortic root >4 cm diameter or a rapidly dilating aorta.<sup>11,12</sup>

### Class 2 and 3 Conditions (Table 3)

- Class 2 conditions: pregnancy presents a small increased risk of maternal mortality or morbidity.

**Table 3** Conditions in which pregnancy is Class 2 or 3

| Class 2 if otherwise well and uncomplicated | Class 2–3 depending on individual  | Class 3 <sup>a</sup>                   |
|---|--|--|
| Unoperated atrial septal defect             | Mild left ventricle impairment   | Mechanical valve                       |
| Repaired tetralogy of Fallot                | Hypertrophic cardiomyopathy  | Systemic right ventricle <sup>b</sup>  |
| Arrhythmias                                 | Native or tissue valvular heart disease not considered Class 4                               | Post Fontan operation <sup>c</sup>     |
|   | Marfan syndrome without aortic dilation (with/without a family history of aortic dissection) | Cyanotic heart disease                 |
|   | Heart transplantation  | Other complex congenital heart disease |

<sup>a</sup>Class 3 unless other risk factors, in which case pregnancy may carry a Class 4 risk.

<sup>b</sup>Congenital heart disease in which the right ventricle supports the systemic circulation.

<sup>c</sup>Fontan operation for tricuspid atresia and other conditions where there is only one functional ventricle. The single ventricle is used to support the systemic circulation. This results in a low cardiac output, hypercoagulable circulation.

**Table 2** Conditions in which pregnancy is Class 4

|  |
|--|
| Pulmonary arterial hypertension of any cause   |
| Severe systemic ventricular dysfunction  |
| NYHA III–IV or ventricular ejection fraction <30%  |
| Previous peripartum cardiomyopathy with any residual impairment of left ventricular function |
| Severe left heart obstruction  |
| Marfan syndrome with aorta dilated >40 mm  |

**Table 4** Conditions in which pregnancy is Class 1

|  |
|--|
| Uncomplicated, small or mild   |
| Pulmonary stenosis   |
| Ventricular septal defect  |
| Patent ductus arteriosus   |
| Mitral valve prolapse with no more than trivial mitral regurgitation |
| Successfully repaired simple lesions                                 |
| Ostium secundum atrial septal defect                                 |
| Ventricular septal defect  |
| Patent ductus arteriosus   |
| Total anomalous pulmonary venous drainage                            |
| Isolated ventricular extrasystoles and atrial ectopic beats          |

- Class 3 conditions: pregnancy presents a significantly increased risk of maternal mortality or severe morbidity. Expert counselling required. If pregnancy is decided upon, intensive specialist cardiac and obstetric monitoring needed throughout pregnancy, childbirth and the puerperium.

Patients with the conditions listed in Table 3 fall into either Class 2 or Class 3 categories depending on individual circumstances; they require individual assessment in a specialist unit. All women with these conditions may go up a class or more if there are additional risk factors such as the need for anticoagulation, or a combination of conditions. For example, pregnancy in a woman with repaired tetralogy of Fallot with atrial arrhythmias and mild left ventricle impairment may be associated with Class 3 risk.

In addition, cyanosis with a pre-pregnancy resting arterial oxygen saturation <85% is associated with only a 12% chance of livebirth,<sup>13</sup> and this fetal risk should also be considered when assessing maternal risk.

#### Class 1 Conditions (Table 4)

- Pregnancy presents no detectable increased risk of maternal mortality or morbidity.

#### Sterilisation

Although sterilisation may appear to be the obvious choice for many women who should not get pregnant, it is rated WHO 2 at best because of the risks associated with the procedure itself, its late failure rate, its psychological impact on the patient, and the availability of secure and safe alternatives.

Late sterilisation failure rates are higher in young women.<sup>14,15</sup> They may result in ectopic pregnancies, the management of which is a major problem in women with heart disease or pulmonary vascular disease, especially if the patient is taking anticoagulants.

For laparoscopic sterilisation under general anaesthetic, the combination of positive-pressure ventilation, abdominal insufflation with CO<sub>2</sub> and intermittent head down tilt all decrease venous return, an effect which is poorly tolerated by those with pulmonary vascular disease or a Fontan circulation (see footnote to Table 3). Use of local anaesthetic is an attractive option in skilled hands, but not for those with pulmonary vascular disease, because of the risk of vagal reactions to which such patients are particularly vulnerable. Patients with right-to-left shunts are also at risk of paradoxical embolism both from air emboli from venous catheters and from the soluble CO<sub>2</sub> used for insufflation.

The safest surgical technique is probably mini-laparotomy or minimal laparoscopy (with <200 ml CO<sub>2</sub> and negligible increases in intra-abdominal pressure). This can be performed using the safest anaesthetic regime for patients with pulmonary vascular disease (i.e. low-dose neuraxial block with combined spinal and epidural block). High-risk patients should receive invasive monitoring in the perioperative period.

Sterilisation can be done at the time of Caesarean section, thus avoiding the risk of a separate procedure. However, the failure rate is higher than when performed as a separate procedure.<sup>15</sup>

The place of the new hysteroscopic sterilisation technique known as Essure<sup>®</sup> is unclear.<sup>16</sup> Special intratubal stents are inserted, usually with no more than oral analgesia, and the risk of vagal reactions may be reduced using the anaesthetic techniques described above. Early efficacy testing at 3 months reports no failures to date.

Vasectomy is rarely appropriate. The male partner of a woman with severe cardiovascular or pulmonary vascular disease is likely to outlive her and may wish to father children with a new partner.

The role of sterilisation has been reduced by some of the reversible contraceptive techniques such as the intrauterine system (IUS) (Mirena<sup>®</sup>) and the subdermal implant (Implanon<sup>®</sup>), both of which are as effective as sterilisation. In addition, some women will not be able to accept the finality of never being able to have children and therefore alternatives to sterilisation are welcome.

#### Contraceptive methods

The principle of 'Summation of Risk' applies to individual contraceptive methods, namely that a contraceptive method should be avoided in general if its adverse effects summate with a known risk of the (heart) disease.<sup>2</sup>

#### Combined hormonal contraceptives

**Combined oral contraceptives.** The combined oral contraceptive pill (COC) is a safe, effective and popular method of contraception. The estrogen component is associated with increased risk of arterial and venous thromboembolism. It is this association that limits the use of the COC in some women with cardiovascular disease (Table 5).

The risk of ischaemic stroke associated with the COC is increased by additional vascular risk factors including smoking, hypertension, diabetes, obesity and migraine, especially migraine with aura.

Women whose cardiac status is prothrombotic may be at particular risk, and careful consideration should be given to the use of the COC as opposed to alternative progestogen-only contraceptive methods. Anticoagulation does not protect entirely against the further thrombotic risk of the combined pill. In addition, both estrogens and progestogens may interfere with warfarin metabolism, so the international normalised ratio (INR) should be monitored more frequently when initiating the COC. Hence, even if a patient is anticoagulated with warfarin the COC would be classified at minimum as WHO 3, usually reverting to WHO 4 if anticoagulation ceases.

Women with right-to-left shunts due to cyanotic heart disease or pulmonary arteriovenous malformations are at risk of paradoxical embolism and stroke if they develop venous thrombosis whilst on the COC; it is contraindicated (WHO 4) in these women. Although an uncomplicated, unoperated atrial septal defect results in left-to-right shunting, it is possible to reverse the shunt with simple physiological manoeuvres (e.g. Valsalva) and so women with atrial septal defect should also consider other forms of contraception, especially if they have additional risk factors for thromboembolism (WHO 3).

Paradoxically, because of its benign nature, advice for women with known patent foramen ovale (PFO) is more complex. Although PFO is associated with embolic stroke,<sup>17</sup> it is a normal variant that occurs in 10–20% of the population, remaining asymptomatic and undiagnosed in



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**Table 5** World Health Organization (WHO) risk classification for the use of combined hormonal contraceptives (i.e. COCs, Evra® and NuvaRing®)

| WHO 1   | WHO 2   | WHO 3   | WHO 4  |
|---|---|---|--|
| Condition with no restriction for the use of the contraceptive method             | Condition where the advantages of the method generally outweigh the risks   | Condition where the risks of the method usually outweigh the advantages: consider carefully all alternatives first <sup>a</sup> | Condition where the method represents an unacceptable health risk                                |
| <b>Always usable</b>  | <b>Broadly usable</b>   | <b>Caution in use</b>   | <b>Do not use</b>  |
| Physiological murmurs in absence of heart disease                                 | Most arrhythmias other than atrial fibrillation or flutter  | Atrial fibrillation or flutter on warfarin <sup>b</sup>   | Atrial fibrillation or flutter, if not anticoagulated  |
| Mitral valve prolapse with or trivial mitral regurgitation                        | Uncomplicated mild native mitral and aortic valve disease   | Bi-leaflet mechanical valve in mitral or aortic position taking warfarin <sup>b</sup>   | Bjork Shiley or Starr Edwards valves even taking warfarin  |
| Bicuspid aortic valve with normal function  | Tissue prosthetic valve lacking any of the features noted in WHO 3 and 4 columns  | Atrial septal defect with left-to-right shunt that may reverse with physiological stress (e.g. Valsalva manoeuvre)              | Pulmonary hypertension or pulmonary vascular disease (e.g. Eisenmenger's syndrome)               |
| Mild pulmonary stenosis   | Surgically corrected congenital heart disease lacking any of the features noted in WHO 3 or 4 columns                   | Repaired coarctation with aneurysm and/or hypertension  | Dilated left atrium >4 cm  |
| Repaired coarctation with no hypertension or aneurysm                             | Small left-to-right shunt not reversible with physiological manoeuvres (e.g. small VSD, small patent ductus arteriosus) | Marfan syndrome with aortic dilatation unoperated   | Fontan heart <sup>c</sup> even taking warfarin   |
| Other simple lesions successfully repaired in childhood and with no sequelae e.g. | Uncomplicated Marfan syndrome   | Past thromboembolic event on warfarin <sup>b</sup>  | Cyanotic heart disease even taking warfarin  |
| Ostium secundum atrial septal defect  | Hypertrophic cardiomyopathy (HOCM) lacking any of the features noted in the WHO 3 and 4 columns                         |   | Pulmonary arteriovenous malformation   |
| Ventricular septal defect   | Past cardiomyopathy, fully recovered, including peripartum cardiomyopathy   |   | Past thromboembolic event (venous or arterial) not taking warfarin                               |
| Patent ductus arteriosus  |   |   | Poor left ventricle function of any cause (e.g. dilated cardiomyopathy) (ejection fraction <30%) |
| Total anomalous pulmonary venous drainage   |   |   | Coronary artery disease  |
|   |   |   | Coronary arteritis (e.g. previous Kawasaki's disease with coronary involvement)                  |

<sup>a</sup>WHO 3: alternatives are usually preferable. Exceptions if: (i) the patient accepts risks and rejects alternatives or (ii) the risk of pregnancy is very high and the only acceptable alternative methods are less effective.

<sup>b</sup>Warfarin: care with monitoring the international normalised ratio (INR), which may alter with both estrogen and progestogen hormone therapy.

<sup>c</sup>Fontan operation for tricuspid atresia and other conditions where there is only one functional ventricle. The single ventricle is used to support the systemic circulation. This results in a low cardiac output, hypercoagulable circulation.

NB. In the presence of any feature listed in the third or fourth columns of the table, the more exclusive category should be applied. For example, mitral valve disease with dilated left atrium moves to WHO 4. Furthermore, the presence of two or more features in the WHO 2 or 3 columns or the addition of an independent risk factor such as smoking or hypertension generally contraindicates combined oral contraceptive use (i.e. WHO 4).

most individuals.<sup>18</sup> Women whose PFO was discovered because of a clinical event such as embolic stroke or neurological decompression sickness after diving should be advised against using the COC (WHO 4). For women in whom PFO is an incidental finding, this working group classifies its use as a 'permissive' WHO 2, since there is a theoretical, but very small, risk of paradoxical embolism. The working group certainly does not advocate screening for PFO in asymptomatic women seeking to use the COC.

**New combined non-oral contraceptives.** EVRA®, a combined contraceptive skin patch, is available, and NuvaRing®, a combined contraceptive vaginal ring, although not yet available in the UK, is licensed in several other countries. Since these methods contain ethinylestradiol and a progestogen (norgestromin and etonogestrel, respectively), similar eligibility criteria – and side effects – apply as for the COC.

### Progestogen-only methods

Contraceptive doses of progestogens used alone are not associated with an increased risk of arterial or venous thrombosis.<sup>19–21</sup> Therefore all progestogen-only methods are usable when there is an arterial or venous thrombotic risk and, broadly speaking, are safe for all forms of heart disease (Table 6). However, progestogens may sometimes interact with warfarin to affect the INR, so additional anticoagulation monitoring should be advised early in their use and when they are discontinued.

### Progestogen-only pills

Progestogen-only pills (POPs), although safe in cardiac disease, are generally not recommended for those with major heart disease (pregnancy WHO Class 3–4) where maximum efficacy is needed.

The new POP, Cerazette® (desogestrel 75 µg), may be extremely useful for women who are unable to take the COC and require reliable contraception.<sup>2</sup> In contrast to

**Table 6** Safety of progestogen-only contraceptive methods in women with heart disease

| Progestogen-only contraceptive method <sup>a</sup> | Cardiac condition  | WHO Class |
|--|--|-----------|
| Standard POP <sup>b</sup>                          | All cardiac patients   | 1         |
| Cerazette <sup>®</sup> POP <sup>c</sup>            | All cardiac patients   | 1         |
| Depo-Provera <sup>®</sup>                          | All cardiac patients not on warfarin   | 1         |
|  | All cardiac patients taking warfarin <sup>d</sup>  | 3         |
| Implanon <sup>®e</sup>                             | All cardiac patients   | 1         |
| Mirena <sup>®</sup> IUS                            | Cardiac patients generally, even if taking warfarin <sup>a</sup>   | 1         |
|  | Structural heart disease <sup>e</sup> , except as below  | 2         |
|  | Prosthetic heart valves <sup>a,e</sup>   | 3         |
|  | Previous endocarditis  | 3         |
|  | Pulmonary hypertension, Fontan circulation <sup>f</sup> , or other condition in which vagal reaction at insertion would be poorly tolerated <sup>g</sup> | 4 (3)     |
| Emergency contraception (Levonelle <sup>®</sup> )  | All cardiac disease <sup>c</sup>   | 1         |

<sup>a</sup>Warfarin: care with monitoring the international normalised ratio (INR), which may alter after initiation of any progestogen hormone therapy. The effect of the exceptionally low levonorgestrel blood levels with the Mirena IUS is unknown, likely minimal.

<sup>b</sup>Although safe, the standard progestogen-only pill is less effective than all the other progestogen-only methods. It should not normally be advised where pregnancy poses a high or unacceptable risk (Class 3 and 4 conditions).

<sup>c</sup>Efficacy reduced by bosentan (see text).

<sup>d</sup>Risk of large haematoma at site of injection.

<sup>e</sup>If used, appropriate parenteral antibiotic cover (see *British National Formulary*) is advised to prevent endocarditis following insertion.

<sup>f</sup>Fontan operation for tricuspid atresia and other conditions where there is only one functional ventricle. The single ventricle is used to support the systemic circulation. This results in a low cardiac output, hypercoagulable circulation.

<sup>g</sup>See text, may be used if no other method suitable and risk of pregnancy outweighs risk of insertion.

IUS, intrauterine system; POP, progestogen-only pill.

older POPs, the primary action of Cerazette is anovulatory. Hence Cerazette has similar efficacy to the COC and a 12-hour 'window' for missed pills.

Because Cerazette is the prodrug for the same progestogen as released by the Implanon implant (see below) it can be useful for trial before the latter, to assess non-bleeding hormonal side effects. Users must be warned concerning the likelihood of irregular bleeding.

Standard POPs are contraindicated (WHO 4) for women receiving bosentan for pulmonary hypertension. Bosentan is an endothelin antagonist and is also an enzyme inducer and may reduce the efficacy of progestogen-only contraceptives. It is extremely important to avoid pregnancy in this group of patients; therefore, on efficacy grounds, Cerazette (at increased dose) would be the only appropriate POP (WHO 3) for use in these women. The Mirena IUS and Depo-Provera<sup>®</sup> are not affected by bosentan, but the working group considered that insertion of Mirena is particularly high risk in pulmonary hypertension and therefore contraindicated (see below).

#### Depo-Provera

This is a highly effective injectable contraceptive method with no cardiac contraindications. To maintain efficacy, compliance with 12-weekly injections is imperative, fertility frequently returning to normal if injections are delayed. Furthermore, the deep intramuscular injections may cause

significant haematomas in those who are anticoagulated with warfarin (WHO 3). Many women become amenorrhoeic with continued use, which is an advantage, especially for women receiving warfarin or with cyanotic heart disease, many of whom suffer from menorrhagia.

#### Implanon

The progestogen (etonogestrel) implant known as Implanon has no cardiac contraindications, is as effective as sterilisation and produces steadier blood levels (and generally fewer side effects) than Depo-Provera. There is much less risk of haematoma formation, as the implant is subdermal and only needs replacing every 3 years. Around 20% of women using Implanon become amenorrhoeic, which is again an advantage for those with menorrhagia.

The efficacy of Implanon is also affected by bosentan, so a supplementary method of contraception (most appropriately Cerazette, which contains the same progestogen) should be used in order to provide secure contraception for women with pulmonary hypertension.

#### Mirena IUS

This hormone-releasing IUS does not have the risks of increased vaginal bleeding and pain that are associated with the older copper intrauterine devices (IUDs); indeed most women become oligo-amenorrhoeic, a major advantage to many women with cardiac disease. The method has a similar efficacy to sterilisation.

As with copper IUDs, there is a risk of infection at the time of insertion, which makes screening in advance for sexually transmitted infection (STI) necessary. The insertion should be covered with antibiotics in those patients with heart disease who are at risk of bacterial endocarditis (as directed by the *British National Formulary*).

The IUS may appropriately be inserted in those who have not had children (WHO 2). For the majority of women with heart disease (not pulmonary vascular disease or the Fontan circulation, see below) the Mirena system may be classed: WHO 1 once successfully inserted; WHO 2 if there is an insertion risk of infective endocarditis (given appropriate antibiotic cover at insertion); WHO 3 in a patient with a prosthetic valve; and WHO 4 if the endocarditis risk is unusually high (e.g. a patient with previous endocarditis).

It should be noted that up to 5% of women experience a vasovagal response at the time the cervix is instrumented for insertion of the device. Such a response carries a significant risk of cardiovascular collapse in those with pulmonary vascular disease or a Fontan circulation (see footnote to Table 3). In the case of pulmonary vascular disease, a vagal reaction may be fatal. The use of atropine does not guarantee safety from vagal reactions. Paracervical block may help to prevent vagal reactions although combined spinal and epidural block may be a better option. Overall, this working group believes that the progestogen implant (Implanon) is a better option to both the IUS and a copper IUD for women in whom vagal reactions carry a risk of cardiovascular collapse. However, if Implanon results in unacceptable bleeding, then the risk of pregnancy in a pulmonary hypertensive woman may outweigh the risk of Mirena insertion by a skilled operator.

#### Standard IUD

Provided a banded copper IUD is used,<sup>2</sup> these have the useful advantage of needing less frequent replacement (10 years in the case of the current 'gold standard', T-Safe<sup>®</sup> CU 380 A) than the Mirena IUS, and may suit women with heart disease if they initially have light and pain-free

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**Table 7** World Health Organization (WHO) Class for contraceptive methods in specific clinical conditions<sup>a</sup>

| Clinical condition  | Combined hormonal methods (estrogen containing) | POP ('minipill') | Cerazette® | Implanon® | Depo-Provera®                   | Mirena® IUS        | Standard IUD | Emergency hormonal contraception |
|---|---|------------------|------------|-----------|---------------------------------|--------------------|--------------|----------------------------------|
| Physiological murmur  | 1   | 1                | 1          | 1         | 1                               | 1                  | 1            | 1                                |
| Paroxysmal AF (even on warfarin <sup>b</sup> ) with structurally normal heart | 3   | 1                | 1          | 1         | 1 (3 on warfarin)               | 1                  | 1            | 1                                |
| Repaired Fallot without complications   | 1   | 1                | 1          | 1         | 1                               | 1                  | 2            | 1                                |
| Unoperated atrial septal defect   | 3   | 1                | 1          | 1         | 1                               | 1                  | 1            | 1                                |
| Dilated cardiomyopathy  | 4   | (1) <sup>c</sup> | 1          | 1         | 1 (3 on warfarin <sup>b</sup> ) | 1                  | 1            | 1                                |
| Moderate aortic stenosis  | 2   | 1                | 1          | 1         | 1                               | 2                  | 3            | 1                                |
| Bjork Shiley mitral valve replacement <sup>b</sup>                            | 4   | 1                | 1          | 1         | 3                               | 3                  | 4            | 1                                |
| Bileaflet mitral valve replacement <sup>b</sup>                               | 3   | 1                | 1          | 1         | 3                               | 3                  | 4            | 1                                |
| Cyanotic heart disease without pulmonary hypertension                         | 4   | (1) <sup>c</sup> | 1          | 1         | 2 (3 on warfarin <sup>b</sup> ) | 2                  | 3            | 1                                |
| Eisenmenger syndrome and pulmonary hypertension of any cause                  | 4   | (1) <sup>c</sup> | 1          | 1         | 1                               | 4(3 <sup>d</sup> ) | 4            | 1                                |
| Fontan circulation even on warfarin <sup>b</sup>                              | 4   | (1) <sup>c</sup> | 1          | 1         | 3                               | 4(3 <sup>d</sup> ) | 4            | 1                                |

<sup>a</sup>See sections of text on specific contraceptive methods for more information.

<sup>b</sup>Warfarin: care with monitoring the international normalised ratio (INR), which may alter with both estrogen and progestogen hormone therapy. With Depo-Provera there is a specific risk of local haematoma (see text).

<sup>c</sup>Although safe, the limited efficacy of the progestogen-only pill limits its use in women in whom pregnancy carries a particular risk (Class 3 or 4, as in Tables 2 and 3).

<sup>d</sup>May be used if no other method suitable and risk of pregnancy outweighs risk of insertion. IUD, intrauterine device; IUS, intrauterine system; POP, progestogen-only pill.

periods. Though WHO<sup>5</sup> itself classifies copper IUDs as WHO 2 in patients with 'complicated' valvular heart disease, this working group has graded copper IUDs WHO 3 because the risk of endocarditis is theoretically likely to be greater than with the Mirena IUS (since progestogenic mucous effects may reduce uterine entry of pathogens).

In those with pulmonary vascular disease, similar constraints apply to insertion as discussed above for the IUS.

The risk of menorrhagia in those who are anticoagulated makes copper IUDs WHO 3 (i.e. even after successful insertion).

### Emergency contraception

This is safe for all women with heart disease (WHO 1) as it contains no estrogen. The licensed formulation is levonorgestrel 1500 µg (Levonelle®) given as a single dose. If initiated within 72 hours of sexual exposure this has overall a 1% failure rate.<sup>2</sup> About 15% of women will experience nausea and 1.5% vomit.

The efficacy of emergency contraception may be reduced in patients on bosentan (see above). If required, the dose should be increased by 50–100%.

Emergency contraception is not recommended as a regular long-term contraceptive technique due to its high annual failure rate, plus its lack of protection against STIs. Indeed, if there is not mutually assured monogamy, all the above methods need supplementation by male (or female) condom use.

### Contraceptive advice for particular clinical situations

When discussing contraceptive options with a woman with heart disease, the first decision is usually whether the COC is safe, as shown in Table 5. Following this, a decision has to be made as to which of the progestogen-only methods may be recommended. Whilst there are no cardiac contraindications to progestogen itself, consideration must be given to the actual method, namely whether there is a risk of endocarditis or haemodynamic collapse at insertion of an IUS, or a risk of haematoma with Depo-Provera

injection. In addition to safety, the efficacy of the contraceptive method should be considered; for example, although safe, the low efficacy of the POP 'minipill' means it is not a desirable choice for women in whom pregnancy carries a very high risk.

Table 7 illustrates the relative advisability of different contraceptive methods for particular difficult or common clinical situations.

### Conclusions

This review aims to offer practical guidance for clinicians including cardiologists, obstetricians, general practitioners and family planning experts in order that the increasing numbers of women with heart disease can gain access both to safe and reliable contraception and to advice about their risks in pregnancy.

Inevitably the suggested gradings for pregnancy and contraception are arbitrary. They are based on the evidence available when this review was written, and on expert clinical opinion with assessment of the natural history and particular risks associated with each condition. There could be much more confidence about these gradings if large prospective studies of outcome in various forms of heart disease using different contraceptive methods were available. There is a real need for such studies.

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