The Denolin Lecture

The woman with congenital heart disease*

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Introduction

Congenital heart disease, the main concern of paediatric cardiology, now presents problems for adult cardiologists, untrained and uninterested in such patients. Paediatric cardiology, stimulated by the challenge of cardiac surgery for congenital anomalies, has focused on anatomical disorders, changing nomenclature (often), embryological ‘myths’ and the results of various and many remarkable surgical feats. The latter’s success has created a new medical community — the ‘grown-up’ congenital heart patients — the GUCH. The patients’ gender has not concerned anyone. Whether it influences outcomes or natural history in congenital heart disease is neither known nor discussed.

Since the opening of the adolescent cardiac unit in 1975 at the National Heart Hospital, which expanded into the GUCH unit now in the Royal Brompton, a database has been developed over the 20 years. This contains information on more than 5000 GUCH patients, and provides the basic data for this lecture.

As a specialist unit within Cardiology there is bias for referral of complex problems which influence statistics, sometimes giving too gloomy a picture. Certainly the care of and provision for GUCH patients includes all teenagers (adolescents) and adults for their full life span, irrespective of gender. Whether gender influences outcomes and problems will be examined.

The data on prevention and treatment of coronary heart disease and hypertension in men do not automatically apply to women. A woman is not an honorary man. By definition in the Shorter Oxford English Dictionary (1956) a woman is ‘an adult female human being’, additionally with secondary definitions ‘a female servant’, ‘a mistress’, ‘a wife’ and ‘the reverse of a coin referring to Britannia’. A female belongs to the sex which bears offspring — it is this characteristic which makes a woman different from a man.

A child becomes an adult when reaching a particular age, which varies from country to country, defined for the law, for health management, government, etc. Adolescence and adolescents are not recognised officially in the United Kingdom’s Department of Health; one is either a child or an adult at age 16 years. Since a female can and does bear children before the age of 16 years it is difficult to know when womanhood begins from the definitions.

Gender incidence of congenital cardiac anomalies

The old textbooks of paediatric cardiology and congenital heart disease, particularly Keith, Rowe and Vlad[1] provide us with knowledge of the incidence of the various anomalies. Four lesions appear to be more common in the female — mitral valve prolapse, secundum atrial septal defect, persistent duct (provided it is not caused by rubella when it is equally distributed between the sexes), and common atrium; all conditions affecting the inflow of the heart. Male dominance occurs in transposition of the great arteries, aortic valve stenosis, coarctation, univentricular hearts, Fallot’s tetralogy and total anomalous pulmonary venous drainage. Other lesions, including those that are rare, appear to be equally distributed between the sexes. Pulmonary valve stenosis has an increased incidence in males when born in the autumn (conceived in the winter) and an increase in females born in the spring (conceived in the summer)[2]. The result is that there are more males with congenital heart disease, in part explained by the relative frequency of the male dominated aortic valve disease and coarctation.
Gender of GUCH hospital population

Statistics from the GUCH database probably represent 90–95% of GUCH patients in the National Heart and Royal Brompton Hospital, but do not include the adults attending the outpatients of paediatric cardiology since they are unknown to the GUCH unit. The gender of the GUCH patients over 20 years with various congenital heart problems is shown (Figs 1(a) and (b)). The gender distribution is the same as in earlier life, suggesting that gender in childhood does not influence survival. As expected, there is an increase in males with aortic stenosis and Fallot’s tetralogy.

However, when it comes to the ‘Eisenmenger reaction’ — a physiological, not an anatomical state of raised pulmonary vascular resistance and cyanosis from balanced or reversing shunt [3], which includes many different types of defect — there is a higher percentage of females. There is a possibility that there is a predisposition to elevated pulmonary vascular resistance in the female compared to the male, which is established for unknown reasons in childhood and puberty. Although there is an increased incidence of atrial septal defect in the females who are survivors, this cannot be the only explanation, since atrial septal defects per se uncommonly have early pulmonary vascular disease, and ventricular septal defects were commoner amongst the cohort of Eisenmenger patients. The gender incidence over 40 years shows that only 25% of the Eisenmenger group are female (Fig. 2). This ‘disappearance’ is explained by increased deaths of the female Eisenmenger (Fig. 3) between the ages 20–39 years, which also occurs in tricuspid atresia with simple palliation, Fontan-type procedures and the rare patient who survives with no earlier intervention. Such figures suggest that gender may influence the timing of death in certain adult congenital heart anomalies.

Death and gender

The causes leading to death in patients with the Eisenmenger reaction are shown (Fig. 4). More female patients die at mean age 29.4 years. Pregnancy, extracardiac surgery with complications related to gynaecological surgery, and cerebral abscess contributed to the increased female mortality prior to age 40 years. However, whether hormonal fluid retention and predisposition to thrombosis might have contributed, is still only speculation.

Without doubt, being female carries special risks when there is serious pulmonary vascular disease in comparison to males with comparable disease and defects.
Death in coarctation of the aorta, operated and unoperated, is not increased in females aged 20–40 years, despite there being many pregnancies completed with success. Death in coarctation is mostly related to surgery (re-operation) on associated aortic valve stenosis or regurgitation, and so is much more frequent in males as there are more men with coarctation and aortic valve disease.

In a series of 269 patients (165 male, 104 female) having had radical repair of tetralogy of Fallot, symptomatic ventricular tachycardia and sudden ‘unexpected’ death, not necessarily from ventricular arrhythmia, were a frequent cause of death and morbidity in males, yet exceptional in the females. Is this chance or an hormonal effect? Females with repaired Fallot had a higher incidence of death related to pulmonary vascular disease after shunts, and suicide, not encountered in males.

In a series of Fontan-type procedures (19 male, 20 female) who survived beyond 10 years there was no gender difference in complications or deaths.

More attention to gender in judging results and prognosis of cardiac surgical procedures is needed. Since gender does not receive attention in surgical series it will never be seen to influence outcomes.

**Lifestyle factors**

Many of the demands and lifestyles of women potentially affect their health adversely. The unique influence of hormonal factors in the female, as well as demands by society and the woman herself, create many differences from the male and these have potential and actual effects on women’s heart problems in certain circumstances.

**Contraception**

Each form of contraception can solve as well as create problems. Advice is a matter of balancing problems of the contraceptive method against risk of pregnancy. The AIDS epidemic and the male’s need to protect himself has reduced the problems of contraception for the female. Cardiologists are poor at advising GUCH patients and usually do not pre-empt the problem. It requires to be discussed before unwanted pregnancy occurs. In the case of ‘children’ this discussion should take place in the absence of a parent, who often insists on being in the room, as they always have been with their child. It is often more difficult for paediatric cardiologists, generally, to provide adequate advice as they neither have training nor experience in this field. On the other hand, gynaecologists, fearing the heart problems, are often reluctant to advise, thus returning the problem to the cardiologist or general practitioner. Contraindications of various methods are often explained by the latter two, but good advice does not necessarily follow so the patient remains confused and unprotected. Intra-uterine devices may be adequate, but have a definite small risk of causing endocarditis at insertion, bleeding, sepsis and unexpected pregnancy. The low oestrogen pill is excellent but its side effects of fluid retention, thrombosis, upset in anticoagulants, raised blood pressure, may cause problems in certain GUCHs. In cyanotic patients on such a pill, there is an incidence of thromboembolic events within the first 6 months of taking it and thus patients should be warned about this complication, which has occurred in about 15% of GUCH patients. If the risks of the low oestrogen pill are acceptable in a cyanotic patient then aspirin should be taken at the same time. Because of the thromboembolic risk, the low oestrogen pill is probably contraindicated in cyanotic patients. Since there is some
evidence that pulmonary vascular disease worsens, it is safer not to use it after defect closure in the cyanosed with Eisenmenger reaction and acyanotic patients with residual pulmonary hypertension. Oestrogen pills upset warfarin control, which means dose adjustment is important in those with prosthetic valves; dramatic haemorrhages and lack of adequate control have occurred in the first few months of taking oestrogen pills for contraception.

The progesterone pill may be adequate, possibly has a thrombotic tendency in the polycythaemic cyanotic, but the main problem is that patients can feel unwell and develop lumpy, spotty skins.

However most female GUCHs can be treated as normal. It is only those with pulmonary hypertension, the cyanotic, those with valve replacements and heart failure who have particular risk. Those with hypertension may have increased blood pressure, but it is exceptional for those with coarctation or residual hypertension after resection to have a problem. However, they require blood pressure supervision when taking oestrogen contraception. The importance of early planning for the individual cannot be over-emphasized. Effective contraception must be balanced with safety for that patient. Sterilization of the male in the partnership, unless he has already had children and is old enough to be sure he does not want any more, is wrong, particularly when the female has an uncertain prognosis as in the Eisenmenger syndrome. Unfortunately, physicians are still recommending this course. Vaginal sterilization for the woman is a better option, carrying a small risk of death in those where it is most needed, namely the pulmonary hypertensive and Eisenmenger patients. Any difficulties of contraception are outweighed by the problems created by an unwanted pregnancy.

**Pregnancy**

Pregnancy poses more problems in the ‘at risk’ GUCH than the side effects of any form of contraception. Heart disease in pregnancy occurs in only 1% of the obstetric population, but is the prime cause of non-obstetric death; 70–80% of heart disease in pregnancy is now from congenital heart disease because of the increasing GUCH population.

Dr Presbitero and this author joined data[4], studying 416 GUCH patients who had 822 pregnancies and found 59% had successful outcome with live, normal children; this included a high percentage of mothers with complex cardiac problems both operated and unoperated. There was a higher incidence of miscarriages compared to the normal population. Termination was performed in 10% and there was a high incidence of premature live babies.

There are a number of problems to be dealt with in an orderly manner in GUCH mothers (Table 1). Risks to the fetus of the mother with congenital heart disease are death, dysmaturity, prematurity and congenital abnormality. The incidence of congenital abnormalities varies according to the lesion; certain syndromes in mothers have a 90% likelihood of recurrence, as in Noonan’s syndrome, particularly if the potential father is similarly affected. All GUCH pregnancies, particularly those at special risk, need the fetal heart scanned by an expert after 14 weeks and repeated if there is uncertainty or lack of good views. Mothers have a much greater risk of producing affected offspring than the affected fathers. The risk of a GUCH mother having an abnormal fetus may be 4–6 times normal. It is inadvisable to allow a GUCH mother, herself at risk to complete a pregnancy, not to have exact knowledge of the state of the fetus if the abnormality is bad. With identified heart disease, advice about the need for termination and the outcome of fetuses varies according to the advising counsellor. The presentation of the facts depends upon who gives it. A cardiac surgeon, happy with ‘his’ results, is encouraging about prognosis[5], whilst a GUCH doctor or paediatric cardiologist, particularly the former, may be less positive about the future and recommend termination. Since this is about gender issues, I believe men should not be the only advisors to prospective mothers; they do not rear the children nor live with them day by day. Counselling about termination of pregnancy should include the advice of a woman, preferably one who has experience of pregnancy and child care.

Complications of pregnancy in mothers with congenital heart problems vary. Most conditions (Table 2) are associated with normal pregnancy and outcome.

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**Table 1 Problems to be dealt with in GUCH patients concerning pregnancy**

<table>
<thead>
<tr>
<th>Problem</th>
<th>Advice</th>
</tr>
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<tbody>
<tr>
<td>Full cardiovascular assessment prior to pregnancy</td>
<td>Assess risk category</td>
</tr>
<tr>
<td>Assess risk category</td>
<td>Risk of abnormality in fetus</td>
</tr>
<tr>
<td>Risk of abnormality in fetus</td>
<td>Experienced fetal scan for cardiovascular and other abnormality</td>
</tr>
<tr>
<td>Experienced fetal scan for cardiovascular and other abnormality</td>
<td>Type of delivery and where</td>
</tr>
<tr>
<td>Type of delivery and where</td>
<td>Risk of endocarditis</td>
</tr>
<tr>
<td>Risk of endocarditis</td>
<td>Peripartum care</td>
</tr>
<tr>
<td>Peripartum care</td>
<td>Cardiological supervision after (if ‘at risk’)</td>
</tr>
<tr>
<td>Cardiological supervision after (if ‘at risk’)</td>
<td>Future pregnancy advice, including contraception</td>
</tr>
<tr>
<td>Future pregnancy advice, including contraception</td>
<td></td>
</tr>
<tr>
<td>N.B. Important to have cardiologist, obstetrician, anaesthetist and neonatologist working as a team.</td>
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</tbody>
</table>

**Table 2 Congenital heart lesions which can be managed normally during pregnancy**

<table>
<thead>
<tr>
<th>Lesion</th>
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<tbody>
<tr>
<td>Bicuspid aortic valve</td>
</tr>
<tr>
<td>Mild aortic valve stenosis</td>
</tr>
<tr>
<td>Pulmonary valve stenosis (± valvotomy)</td>
</tr>
<tr>
<td>Atrial septal defect (pre and post-operatively)</td>
</tr>
<tr>
<td>Ventricular septal defect (small or closed)</td>
</tr>
<tr>
<td>Mitral valve prolapse</td>
</tr>
<tr>
<td>Well repaired Fallot</td>
</tr>
<tr>
<td>Ductus (small, moderate or closed)</td>
</tr>
</tbody>
</table>

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The physiological changes in the cardiovascular system which occur in pregnancy have deleterious effects in certain conditions. Heart failure always worsens with the increased volume load, which is partly balanced by the help from vasodilatation. Cyanosis increases with the vasodilatation and severe stenotic lesions produce worsening symptoms. Valve regurgitation is usually well tolerated but in all there are increased risks of thromboembolism with necessary rest, and always worsening of established pulmonary vascular disease (pulmonary hypertension). There is a low risk of bacterial endocarditis, but this does necessitate prophylaxis managed by intravenous amoxycillin when the membranes rupture.

Those conditions at special risk are shown in Table 3. For these patients special planning is mandatory and must involve the anaesthetist, cardiologist and obstetrician. Ideally full diagnosis should be made and any necessary cardiac surgery performed before pregnancy. If a lesion becomes critical during pregnancy, surgery should be postponcd until after the birth, but if such a delay is not possible, the best time for surgery is 26–32 weeks. A planned normal vaginal delivery is best, unless there are obstetric complications or particular conditions which require early elective delivery by caesarean section. Good planning for the ‘at risk’ GUCH can be difficult to achieve, particularly in countries where purchasers/provider contracts or health maintenance organizations ‘control’ care. Neither system wants the patient to go outside the prescribed referral centre, even if there is no experience in GUCH management. GUCH patients must be taught to fight for their optimal care. In some, there may be only one chance for a successful pregnancy.

Thus a GUCH unit requires, as a mandatory part of the service to this special medical community, an ‘at risk’ pregnancy service. A prospective study of the first 40 patients from GUCH with shared care* included six with aortic stenosis, hypertrophic cardiomyopathy (four), Marfan, Eisenmenger (one), ‘Mustard’ patients, repaired Fallot, aortic regurgitation and other rare lesions. There was one maternal death (in the Eisenmenger patient) and one dead baby (in a patient with aortic stenosis).

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![Figure 5 Incidence of live births related to resting systemic arterial oxygen saturation at beginning of pregnancy. From Presbitero et al. Circulation 1994; 89: 2673–6.](image)

**Cyanosed patients (without pulmonary hypertension)**

Cyanotic patients have a high fetal loss\(^6\). Spontaneous abortion is related to the level of systemic oxygen saturation; below 85% early fetal loss is likely and above is uncommon (Fig. 5). This simple finding enables the cardiologist to counsel patients about outcome of pregnancy.

Babies born from a blue mother are frequently premature and small for dates. Since cyanosis worsens through the pregnancy, rest is important in order to maintain the oxygen saturation as high as possible. With rest, not in bed, fragmin should be given. Maternal death in cyanotics is unusual. Only one in this series died, one month after the birth, from endocarditis which developed on the Blalock shunt and caused rupture of an aneurysm; she had a badly managed, difficult delivery without prophylaxis. Complications occurred in 30%, all easily treated. It is likely that the incidence of congenital heart disease in the offspring of cyanotic mothers has been underestimated since it may have been present in some of the miscarriages.

Comparisons of the outcomes of pregnancy in cyanosed patients and those acyanotic after repair of the lesions show low maternal mortality in both groups, a greater number of live born infants in the ‘pink’ mothers and far fewer maternal complications. The numbers of offspring with cardiac defects were the same which suggests that genetics may be the main determinant rather than the presence of cyanosis.

**Cyanosis with pulmonary hypertension (Eisenmenger)**

Pulmonary hypertension with cyanosis presents a different and disastrous outlook. A retrospective review (with three prospective cases) of outcomes of 34 pregnancies in 22 patients (from Royal Brompton and Turin) with Eisenmenger reaction showed that in seven patients with
eight pregnancies which continued, two died and four patients deteriorated after. Six patients had caesarean section early, as an emergency in two. All babies had low for dates birth weight and two had congenital heart defects. Efforts were always made to terminate pregnancies, which were performed with few complications in eight; seven had spontaneous abortions.

Deaths did not appear to be related to thromboembolic problems, but in three with necropsy there was diffuse fibrinoid necrosis of pulmonary arterioles leading to the inexorable downhill course after delivery. The only hope is lung transplantation which is usually an impractical solution.

All who survived had clinical deterioration compared to the pre-pregnancy state which suggests pregnancy worsened the prognosis. This author believes that pregnancy is absolutely contraindicated in patients with the Eisenmenger reaction. If the mother insists on continuing with the pregnancy, optimal in-hospital conditions are early delivery by caesarean section with epidural anaesthesia as soon as the child is ‘safe’; warning of responsibility of child care to father and both families is important. Despite acceptance prior to delivery, the child of the dead mother may be abandoned in hospital.

Pulmonary hypertension — acyanotic

The disastrous outcomes of pregnancy in primary pulmonary hypertension are known and it is a condition in which pregnancy is absolutely contraindicated. Some of the deaths where the diagnosis has been Eisenmenger with ‘small atrial septal defect’ are probably primary pulmonary hypertension with stretched foramen ovale. More difficult and with unpredictable outcome are those GUCH women with residual pulmonary hypertension after earlier closure of a defect; the risks start when the pulmonary artery pressure is more than 50% of systemic pressure. A prospective study of outcomes of pregnancy in such patients has not been done. This author has had only four patients with pulmonary artery pressure 50–75% of systemic pressure prior to pregnancy. One died from careless obstetrics (Table 4), reported in the official Maternal Death Census as death from congenital heart disease, but the report neglects to state the cord was pulled in the third stage after a long labour and the patient collapsed! Three delivered live babies early and all had higher pulmonary artery pressures in the post-pregnancy year than before the pregnancy. This suggests that pregnancy accelerated deterioration and carries risks in otherwise asymptomatic patients. Whether it applies to all women with residual moderate pulmonary hypertension after cardiac surgery is unknown.

Table 4 Case report of a GUCH patient aged 22 years who had had repair of double outlet right ventricle age 12 years and had residual pulmonary hypertension

| Pulmonary artery pressure raised 70/30 mmHg, >60% systemic. Appeared pregnant and refused termination. Local obstetrician declined referral outside region. Special risks and needs explained by cardiologist. When 37 weeks pregnant the patient complained of tiredness. Labour was induced on a Friday evening. On Saturday morning, without consultant supervision, midwife and new junior registrar delivered a 7 lb baby. In third stage the cord pulled to remove the placenta. The patient collapsed and had a cardiac arrest. The cardiologist was called (for the first time!) but patient was unresuscitatable. |

Aortic stenosis

This is probably the commonest lesion in the pregnant ‘at risk’ congenital heart population, despite the condition being more common in the male. In the GUCH joint series there were 58 patients with significant aortic stenosis who had 129 pregnancies: 50 (86%) had aortic valve stenosis, important in 14 with a resting gradient >50 mmHg at start or prior to pregnancy. This is the most important fact since the measured gradient doubles after the 13–15th week and is not a true reflection of the severity of the obstruction. Patients with gradients below 60 mmHg had no problems unless there was associated anaemia, infection, pre-eclampsia, or poor obstetrics. Those with severe aortic valve stenosis develop pulmonary oedema if not closely supervised. In three with pulmonary oedema after the 25th week, intravenous diuretics and rest controlled the situation until delivery by caesarean section when the infant was viable. Surgery is possible during pregnancy and avoids the dangers at delivery. Alternative therapy is catheter intervention, which can be performed by covering the abdomen all round with lead and has been successful in one patient at 32 weeks whose valve was domed and pliable without aortic regurgitation.

Subaortic stenosis, where the gradients vary in the same patient, had no problems in pregnancy, except one with very severe concentric hypertrophy who developed runs of ventricular ectopy at 34 weeks and breathlessness responding to rest and small doses of diuretics; she was delivered by caesarean section at 37 weeks.

Coarctation of the aorta before and after resection does not usually have a problem. If anti-hypertensive therapy is used it is important not to reduce pressure beyond the coarctation excessively, otherwise miscarriage may occur. There is a small risk of aneurysm formation and rupture during pregnancy. Note must be taken of new upper thorax back pain. One difficulty is that the definitive investigation, MRI, may not be possible because of the size of the patient and inability to lie on back in the scanner.

Fontan

Although Canobbio and Mair in a series collected from several centres reported good outcomes are
possible with small babies, the author has some reservations as pregnancy and Fontan are prothrombotic. In two pregnancies from a series of 26 patients both had thromboembolic complications from right atrial thrombus and one died from embolic obstruction of the connection two weeks after delivery.

**Valve replacements**

Pregnancy in patients with prosthetic and mechanical valves is more common in patients with rheumatic heart disease. The problems relating to anticoagulants, which are potentially teratogenic, cause haemorrhage and if reduced may permit thromboembolism, have not been solved. Heparin throughout pregnancy, even if controlled by KCT estimation, which is usually not done, is not a sufficient anticoagulant to prevent thromboses on valves and the dose of warfarin needs to be lessened to prevent flagrant embryopathy, although probably milder effects still occur. The accelerated disintegration of bioprostheses in pregnancy is concerning. The question of which valve to use in a young female child/adolescent must include consideration of the risks for future pregnancy. When the congenital mitral valve, or in Marfan’s syndrome needs replacement, a valve requiring anticoagulants cannot be avoided. However when the aortic valve is replaced there are other possibilities such as the aortic homograft and the pulmonary autograft. The homograft in the right ventricular outflow tract, used widely in many complex anomalies, is not affected in pregnancy. In a study by Dore and Somerville on 27 females who had pulmonary autograft replacement, only eight had pregnancies and were normal in all respects. Possibly there was minimal increase in mild right homograft stenosis and calcification, but no changes occurred in the autograft replacing the diseased aortic valve. Since the valve is ‘living’, this is not surprising. This would appear to be the ideal aortic valve replacement for the young female but one needs the ideal surgeon since this is technically demanding surgery requiring experience and dexterity. The choice of valve replacement and the effects of pregnancy must be taken into consideration in female children. Autografts and homografts have an immediate advantage of not needing anticoagulants, and degeneration is not accelerated.

All patients with a systemic right ventricle may show a tendency to fail during pregnancy, with pulmonary oedema during delivery. This can be treated and usually pre-empted by careful pre-delivery and last trimester management. Those at special risk are patients who have transposition treated by Mustard/Senning and those with corrected (congenital) transposition, operated and unoperated, in whom the systemic ventricular (right) function may worsen.

After the pregnancy is completed, the clinical responsibility is not finished for the GUCH patient. Sometimes in certain conditions the cardiac function does not recover to its pre-pregnancy state and may even worsen after the ‘stretching’. The new GUCH mother has more responsibility now the child is born and demanding, and this contributes to deterioration of a diseased heart. Thus the cardiologist must anticipate this and initiate appropriate therapy early. Deterioration occurs, particularly in those with impaired function before, as in systemic right ventricle, dilated cardiomyopathy, and always in those with pulmonary hypertension.

**Gynaecological surgery**

Termination, hysterectomy and sterilization may be required. Gynaecologists tend not to seek advice about the care unless the patient is blue, symptomatic or insistent. Deaths do occur unnecessarily and there have been thromboembolic complications in the cyanotics who, like the pulmonary hypertensives and heart failure patients, require cardiology first, familiar anaesthetists and fragmin for the period of immobilization and at least 2 weeks after.

**Hormone therapy**

Problems arise from hormone administration particularly in the cyanosed, the pulmonary hypertensive, borderline heart failure and those with predisposition to arrhythmia. Hormones of various sorts are needed by the female GUCH (Table 5). Besides contraception, the problem of in-vitro fertilization (IVF) and variations for egg harvesting are arising now with greater frequency, added to by the desire for surrogate pregnancies. Clomiphene is a danger for the cyanotic and pulmonary hypertensive, and has precipitated problems such as atrial fibrillation, heart failure and increasing cyanosis in six consecutive patients. Such patients should be strongly counselled against embarking on these activities. Danazol, used for endometriosis, may make the patients vomit and feel unwell. It is important to check electrolytes, particularly if the subjects are taking diuretics, as hypokalaemia with resultant arrhythmias causes severe problems in a number of conditions.

There is nothing known about post-menopausal hormone replacement in the ‘at risk’ group of patients.

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**Table 5 Hormone treatment sometimes required in female GUCH patients; these may have deleterious effects in certain diseases**

<table>
<thead>
<tr>
<th>Hormone Treatment</th>
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<tbody>
<tr>
<td>Danazol</td>
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<tr>
<td>Oestrogen contraception</td>
</tr>
<tr>
<td>Progesterone</td>
</tr>
<tr>
<td>Clomiphene</td>
</tr>
<tr>
<td>Hormone replacement therapy</td>
</tr>
<tr>
<td>Thyroid (for ‘hypo’ and ‘hyper’, particularly with chronic amiodarone therapy)</td>
</tr>
</tbody>
</table>

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who have survived to the age where they might need it. Without doubt osteoporosis occurs particularly in small slender women and protection from this would be desirable. However, whether the increased risks of thrombosis and fluid retention should be taken in Eisenmenger patients and others with chronic cyanosis remains to be shown. Problems of physical and sexual immaturity are probably commoner than thought in GUCH and may require hormone help but much more investigation is needed. The giving of growth hormones to change the shape may also change the heart. Usually dwarfism is part of syndromes rather than attributable to the heart alone. However children in chronic heart failure are small and might be helped by growth hormone.

Besides the female sex hormones, thyroid disease is important, affecting women more than men. Amiodarone-induced thyrotoxicosis also affects women more than men. If only specialists in other fields could be persuaded to consult and share the GUCH problems there would be fewer unnecessary upsets in GUCH lives.

Lifestyles and responsibility

Inevitably and correctly responsibility for home and family is the woman’s. This, together with women’s constant feeling of guilt (part of the gender), imposes further pressures on the GUCH woman already afflicted with reduced effort tolerance. A study of habits in complex GUCH patients shows that smoking is uncommon, particularly in the female GUCH, and drug and drink abuse are rare, although 15% had taken recreational drugs; of these, the majority experimented with cannabis. Data from a Toronto General Hospital survey showed more female GUCHs remained unmarried compared with male GUCHs and normals, and there was a higher incidence of divorce in female GUCHs compared to male GUCHs. The males tend to leave the female GUCH, particularly when cyanotic, and when multiple hospital admissions and problems with pregnancy occur, although there are some incredible exceptions. In a study of major concerns of GUCH patients with complex heart disease comparing both genders, the females most fear deteriorating health and sudden death whereas the males rarely worry about sudden death or anything in relation to their cardiac health. It is possible that they will not admit anxieties and that this is male bravado. Concerns which the GUCH population voice to the GUCH departmental secretaries (via the telephone) are more frequent in the female compared with the male about every feature of life (Fig. 6). Such concerns should be channelled to the GUCH Patients’ Association.

Appearance

Major problems in relation to appearance are voiced by females. Cardiologists should be sensitive to these. Concerns are about physical immaturity, spotty cyanotic skin, abnormal breast development, badly placed scars, kyphoscoliosis, obesity (rare) and use of slimming tablets. The skills of the plastic surgeon are often needed and should be encouraged if the ugly residuum of life saving surgery can be improved. Much of this could have been avoided with more consideration of the future needs of the female child.

Scoliosis in the general population is commoner in the female and much commoner in the female GUCH. This is an important cause of distressing deformity and many need help, despite the frequent association of serious congenital heart disease.

The taking of slimming pills is a habit of females (rarely of males) and is dangerous for those who have potential to develop pulmonary vascular disease. It may be the cause of irreversible pulmonary vascular disease, complicating a simple atrial septal defect after taking it for only a month. The question of whether slimming pills have been taken should always be explored in GUCH patients.

It is appropriate to remind physicians that the body mass of females is less than the male and considerably less in many female GUCHs. Thus, drug dosages must be adjusted — female GUCHs are often intoxicated by the ‘adult’ dose of drugs because of thoughtless prescriptions.

Advantages

Having considered some of the difficulties and disadvantages of being a GUCH woman, it is important to consider possible advantages.

Coronary artery disease causing symptoms and occasionally needing surgery is now manifesting in old
GUCHs, both surgically treated and naturally surviving. It is likely this will increase as the GUCH population ages and the challenge of operating on these already operated, distorted hearts will be big for the cardiac surgeon.

The coronary arteries of cyanotic patients are large — whether those of the female are even bigger is unknown, but certainly acquired coronary heart disease is exceptional in such surviving blue female patients and only occasionally encountered in the male. Calcification in native bicuspid and mildly abnormal aortic valves appears to occur later in the female compared with the male. Women operated on for calcific aortic stenosis are older in most reported series where they have analysed gender. Re-analysis of data provided by Davies also confirms this (Table 6).

When congenital aortic valve stenosis is critical in infant, child and adolescent, it is not only much commoner in the male but appears more often requiring aortic valvotomy earlier (Fig. 7). Degenerative changes inevitably occur in such valves necessitating re-operation on the calcified aortic valve; the delay between first and subsequent operation is longer in the female compared to males (Fig. 8). Thus, in females overall, it is not only less severe, tending to present later, but takes longer for degenerative changes to require valve replacement. This is a distinct advantage in the natural and unnatural history of a common congenital abnormality. Whether it is due to different calcium metabolism or different lifestyles with less athletic activity is not known.

Aortic homografts, whether used on the right or left side of the heart, degenerate with time, related to several factors such as sterilization method, disease for which implanted, technique etc. Gender of donor and recipient has received no attention. A series of right ventricular to pulmonary artery homografts followed over 30 years from the first case\(^{[11]}\) and females (n=45) with the same homograft in right ventricle to pulmonary artery and re-operation for calcific degeneration. Females appear to be better than males. Unfortunately, there are no data on the gender of the donor valve. ——=women survival; ——=men survival; ———=women original homograft; ———=men original homograft.

<table>
<thead>
<tr>
<th>Gender/number of patients</th>
<th>Age range at operation (years (mean))</th>
</tr>
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<tbody>
<tr>
<td>Bicuspid aortic valve</td>
<td></td>
</tr>
<tr>
<td>Female=110</td>
<td>35-93 (67)</td>
</tr>
<tr>
<td>Male=205</td>
<td>31-84 (64)</td>
</tr>
<tr>
<td>Tricuspid aortic valve</td>
<td></td>
</tr>
<tr>
<td>Female=66</td>
<td>60-95 (75)</td>
</tr>
<tr>
<td>Male=53</td>
<td>49-88 (72)</td>
</tr>
</tbody>
</table>


Figure 7 Percentage of patients in each gender having aortic valvotomy in various age groups from below age 1 year to 29 years. Mean age at operation: male=8-96 years; female=11-62 years. ■=female; □=male.

Figure 8 Time in years after aortic valvotomy in childhood and adolescence when patients needed re-operation for valve degeneration (from increasing calcific stenosis not endocarditis) in males and females. Delay is longer in the females. ■=females; □=males.

Figure 9 Actuarial curve of the survival of males (n=40) and females (n=45) with the same homograft in right ventricle to pulmonary artery and re-operation for calcific degeneration. Females appear to be better than males. Unfortunately, there are no data on the gender of the donor valve. ——=women survival; ——=men survival; ———=women original homograft; ———=men original homograft.

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\(\text{Table 6 Aortic valve replacement for aortic stenosis. The results of re-analysis of the age of adults operated on for replacement of calcified aortic valve. Some with tricuspid valves may not be congenital. In bicuspid and tricuspid valves the females are older.}\)

\begin{tabular}{|l|c|}
\hline
Gender/number of patients & Age range at operation (years (mean)) \\
\hline
Bicuspid aortic valve & 35-93 (67) \\
Female=110 & 31-84 (64) \\
Male=205 & 60-95 (75) \\
Tricuspid aortic valve & 49-88 (72) \\
Female=66 & 31-84 (64) \\
Male=53 & 35-93 (67) \\
\hline
\end{tabular}

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from female donors last longer than those from male donors.

To date it can be said that other factors being more or less equal (disease, pressures, technique), females retain a good functioning homograft up to 30 years, for longer than males, but degeneration cannot yet be prevented.

**Conclusion**

GUCH patients are a small part of adult cardiology. They account for only 6% of the total cardiac medicine and surgery in-patient work where there is a specialist unit, yet consume at least 12% of allotted budget. Female GUCH overall, though fewer in absolute terms, probably consumes more financial, professional counselling etc. resources, because of added problems.

This study suggests that there are important differences between the male and the female GUCHs in certain situations — different cardiac and social problems which may affect prognosis and management — and without doubt the prognosis is worse in the female with certain conditions. Eva Lester wrote in the *British Medical Journal* only ten years ago ‘Thirty full years and ten half years from a good woman makes better economic sense than forty-four years from a less-good man’ which should be remembered when GUCH patients are treated. Considering our patients only as interesting pathology should cease. More attention to gender is needed, not only in management of the infant and child but consideration of their special needs as adults. Maybe if the time honoured gender signs were reversed, so much closer to reality, the correct importance of the female as a patient will be given.

I appreciate the honour which the President and the Board of the European Society of Cardiology gave me in asking me to give the Denolin lecture. It is a privilege. I am sad that Professor Denolin, whom I have known through all the years of my training and practice of cardiology, was unable to be at the Lecture. His distinction and contribution to this Society and Cardiology gives this honour special meaning. I wish to pay tribute to the Working Group on Grown-Up Congenital Heart (GUCH) disease who work so hard in this Society and throughout Europe to improve the care of GUCH patients — a small elite group of patients who need the best treatment that cardiology and cardiac surgery can give but, as yet, do not receive it. It is appropriate that this lecture is given at the first joint meeting of the European Society of Cardiology with the Association of Paediatric Cardiology (AEPc), demonstrating the importance of paediatric and adult cardiology becoming a seamless continuum, yet retaining their independent practices and respect for one another. Each of these specialties, including fetal medicine, must thrive separately but remain closely linked, exchanging knowledge and ideas; what happens in childhood in habits and ill health have much to do with the diseases which manifest later in adult life.

**References**


