

Heart Disease in Pregnancy: Some Controversies

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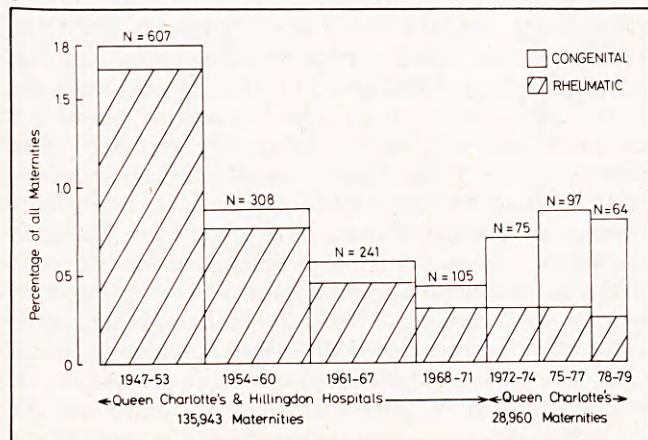
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Examination of the data from Queen Charlotte's Maternity Hospital for the incidence of heart disease in pregnancy (Fig. 1) shows a fall in the incidence of rheumatic heart disease (in 1947-53) from 1.7 per cent to 0.2 per cent of all maternities in 1978-79. Nevertheless, although the incidence of congenital disease was steady at about 0.01 per cent of all maternities between 1947 and 1971, it appears to have risen after 1971. We doubt whether this represents a genuine rise in the pregnant population of the whole UK, even though more children are now surviving surgery for congenital heart disease to enter reproductive life. The published figures for the incidence of heart disease at Queen Charlotte's Hospital between 1947 and 1971[1] include the data from Hillingdon Hospital, because their author was on the staff of both hospitals. After 1971, the figures returned refer to the data from Queen Charlotte's Hospital alone. It is likely that the referral habits of the two hospitals are different, and that diagnostic criteria also change with time; for example, congenital heart disease due to mitral valve abnormalities would not have been diagnosed in the period before 1971. These figures illustrate the difficulty we have in drawing conclusions from incidence data alone.

Fig. 1. Incidence of rheumatic and congenital heart disease in pregnancy, Queen Charlotte's Maternity Hospital, 1947-79.



Bacterial Endocarditis

The diagnosis of heart disease is made more precisely post-mortem and the Confidential Maternal Mortality series of reports gives a more consistent picture of the effect of heart disease in pregnancy. The report for the years 1973-75[2] shows a steady decline in maternal mortality between 1961 and 1975 (Fig. 2). Nevertheless,

Fig. 2. Maternal mortality from heart disease in England and Wales 1961-75[2]. (Permission of the Controller of HMSO.)

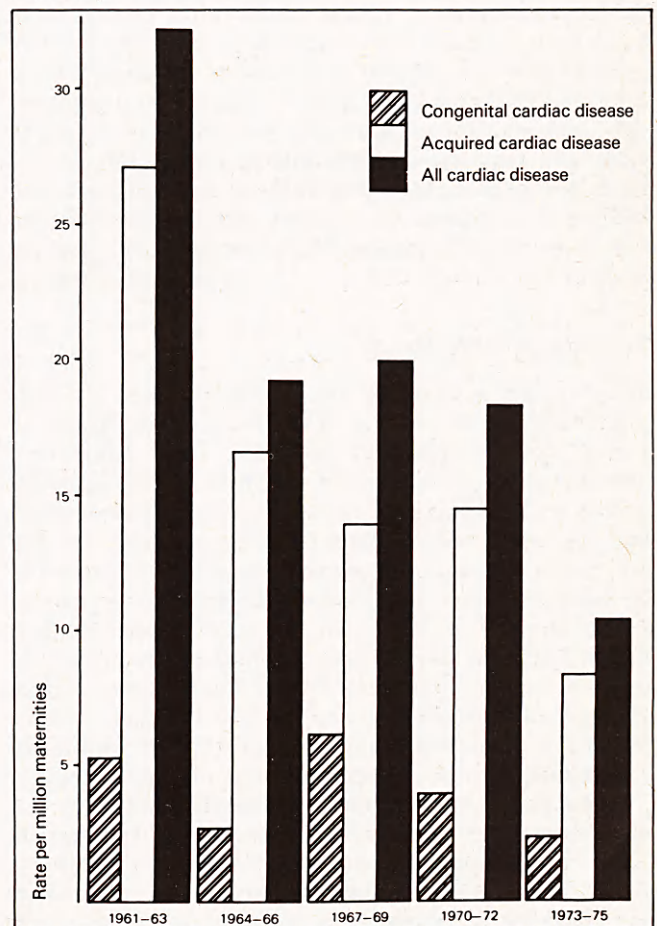


Table 1. Maternal deaths associated with acquired cardiac disease 1970-75[2].

Triennial reports for the years:	Rheumatic valvular disease	Bacterial endocarditis	Coronary disease	Other conditions including cardio-myopathies
1970-72	16	5	4	8
1973-75	3	5	5	3

the table of deaths from acquired heart disease (Table 1) shows a disturbing number of deaths from endocarditis, five in each triennial period 1970-72 and 1973-75. The risk of developing endocarditis in pregnancy is not clearly defined. There is much controversy[3] for[4-6] and against[4,7] antibiotic prophylaxis against endocarditis in labour. There are several large series of patients with heart disease in pregnancy in which no antibiotics have been given[8,9] and in which no endocarditis has been observed. It is difficult[10], though not impossible[11,12], to document bacteraemia in labour. Several authors have argued persuasively against antibiotic prophylaxis[9]. Yet, from the data of the Confidential Maternal Mortality reports, it would seem that women are at risk from endocarditis in pregnancy. What is not clear from these reports is whether the endocarditis was contracted during labour, and was potentially preventable by antibiotics, or whether endocarditis arose at some other time. The one case that is described in detail in the 1973-75 report did appear to develop endocarditis during a normal delivery. Until more details are available, we shall continue to use antibiotic prophylaxis[13], ampicillin 500 mg i.m. and gentamicin 80 mg i.m.[14], 3 injections given eight-hourly at the onset or induction of labour. The patient who is penicillin-sensitive receives one intravenous injection of vancomycin 500 mg, as suggested by Durack[14,15].

Sympathomimetic Drugs

Sympathomimetic drugs are frequently used to stop premature labour[16]. Fig. 3 is the chest radiograph of one of our patients who developed acute pulmonary oedema six hours after delivery. She was a 33-year-old woman with no past medical history of heart disease, who had lost one previous baby from prematurity. In this pregnancy, she again developed premature labour with twins at 27 weeks' gestation. Although the premature labour stopped initially with oral and intravenous salbutamol therapy, it restarted and, in the 24 hours before delivery, she had been given salbutamol 30.5 mg i.v. and 12 mg orally. In addition, she was given dexamethasone 24 mg i.m. in an attempt to induce surfactant formation and reduce the risk of respiratory distress syndrome[17]. The patient was not in positive fluid balance, and the maximum heart rate was 130/min during salbutamol infusion. Although she was initially very sick ($PaO_2 = 7kPa$, 53 mm Hg) she made a rapid recovery after aggressive diuretic therapy.

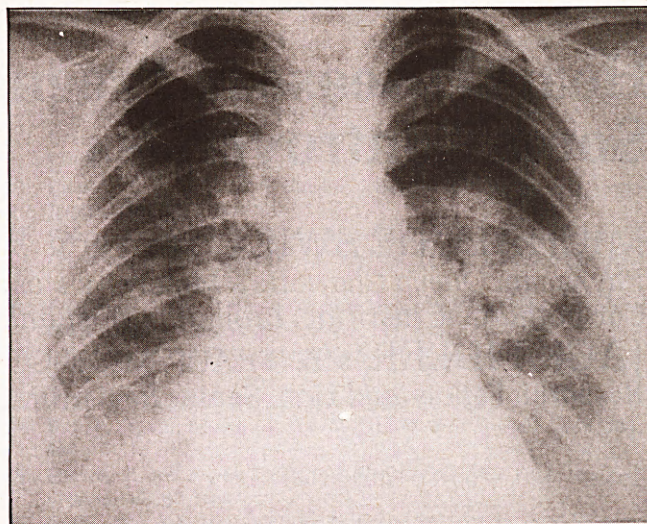


Fig. 3. Chest radiograph of a patient developing pulmonary oedema after treatment for premature labour by salbutamol.

Adverse cardiovascular effects from salbutamol and other beta-sympathomimetic agents given in premature labour have been reported previously, but there is still a general lack of awareness of their importance. Whitehead[18] reported the occurrence of chest pain and ischaemic ECG changes in one patient treated for five hours with intravenous salbutamol (4.2 mg), and subsequently reported pulmonary oedema in another patient given salbutamol 2.2 mg i.v. over six hours[19]. He suggested that vasodilatation caused by concurrent administration of hydralazine and methyldopa for hypertension might be an additional factor increasing circulating blood volume. He also cited[19] one similar case of maternal death reported to the Committee on Safety of Medicines after the use of salbutamol and methyldopa. Davies[20] reported another case of pulmonary oedema after the use of higher infusion rates (20 $\mu g/min$) of salbutamol over a longer period (56 hours). In her case, betamethasone was used, and this may also have increased the circulating blood volume. Davies[20] also suggested that ergometrine given after delivery may have decreased the venous capacitance and thus contributed to the development of pulmonary oedema.

In North America, terbutaline (Bricanyl) is used to treat premature labour. It has the advantage that it can be given subcutaneously. Stubblefield[21] reported one case of pulmonary oedema in which dexamethasone was an additional risk factor. Rogge[22] reported three similar cases and cited knowledge of six others occurring in California. Fenoterol (Berotec) is the most popular beta-sympathomimetic used for premature labour in Germany. Indeed, it is so popular that at one time sufficient fenoterol was prescribed for every pregnant woman in Germany to receive ten 5 mg tablets[23]. Kubli[23] has reported two cases of maternal death associated with the use of fenoterol in patients who had underlying heart disease and cited[23] a further eight cases of pulmonary oedema occurring in Germany before

1977 associated with the use of fenoterol. Ritodrine (Yutopar) is another beta-sympathomimetic that is also used for the treatment of premature labour; pulmonary oedema associated with its use has been reported[24,25].

Beta-sympathomimetics are widely used for the treatment of premature labour[16] even though there are contradictory reports concerning their efficacy[26]. They cause a tachycardia both directly and reflexly because of associated vasodilatation. Both the tachycardia and the increased blood volume associated with vasodilatation may contribute to the risk of pulmonary oedema, particularly if the vascular capacitance is suddenly reduced by ergometrine[20,21,25]. In addition, beta-sympathomimetic agents have metabolic effects; they cause a rise in blood glucose[27] by increasing glycogenolysis and decreasing glucose uptake. Free fatty acid[28] and lactate concentrations[29] increase, and hypokalaemia[27] may occur. These factors may further impair myocardial function in a situation that is already haemodynamically unfavourable. Although it has been suggested that tachycardia alone[30] and/or circulatory overload[31,32] are the real causes of pulmonary oedema in these patients, this seems unlikely. Pulmonary oedema is a rare complication of modern obstetrics, and its occurrence on so many occasions with the use of beta-sympathomimetics suggested that there is specific interaction.

Since there is no universal belief in the efficacy of beta-sympathomimetics, and because of the maternal risk, we would suggest the following guidelines concerning their use for preventing premature labour. Beta-sympathomimetic infusions should not be given for more than 24 hours, except in exceptional circumstances. The risk of cardiovascular adverse effects increases when infusions are given for more than 24 hours, and our clinical impression is that beta-sympathomimetics are less likely to be effective in their curtailment of premature labour if they have not succeeded within 24 hours. Beta-sympathomimetic drugs should be given with great care to patients with pre-existing heart disease. The nature and severity of the heart disease are obviously critical; for example, there would probably be no additional risk of giving salbutamol to a patient with mild mitral regurgitation, whereas such therapy could be fatal in a patient with severe mitral stenosis.

In the presence of maternal diabetes, beta-sympathomimetic infusions can cause gross diabetic ketoacidosis[33] by the mechanisms outlined above. We do not think such severe acidosis and hyperglycaemia can necessarily be prevented by the most aggressive insulin therapy. Once again, because of the lack of proof of universal efficacy, and because of the additional myocardial depression that would be caused by acidosis, we would not use beta-sympathomimetic drugs in maternal diabetes.

If beta-sympathomimetic drugs are used, the obstetrician should be aware of the risk of other therapies. Glucocorticoids will exacerbate hyperglycaemia as well as possibly causing an increase in circulating blood volume due to associated mineralocorticoid activity. This will be exacerbated by vasodilator drugs, so scrupulous attention must also be paid to fluid balance and the maternal heart rate.

Eisenmenger's Syndrome

The congenital defect that has been associated with the highest maternal mortality between 1961 and 1975[2] is Eisenmenger's syndrome.

This mortality has been shown retrospectively to be about 30 per cent[34,35]. Although a series of 23 pregnancies has been reported with no maternal mortality[36], this is likely to be fortuitous and the author could not account for the good results.

Most patients with Eisenmenger's syndrome die in the puerperium. Although deaths are occasionally sudden, due to thromboembolism, they are not usually so. More frequently these patients die because of a slowly falling PaO_2 with an associated decrease in the cardiac output. A consideration of the haemodynamics involved (Fig. 4)

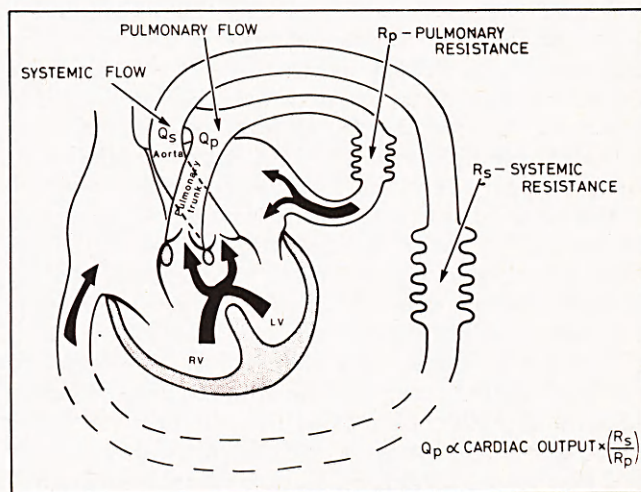


Fig. 4. The heart and circulation in Eisenmenger's syndrome due to a large ventricular septal defect. In this condition the ratio of pulmonary blood flow (Q_p) to systemic blood flow (Q_s) is inversely proportional to the ratio of pulmonary vascular resistance (R_p) to systemic vascular resistance (R_s).

suggests how this might occur and how it could be managed. In a large ventricular septal defect the blood is freely mixed in the right and left ventricles, and the ratio of blood flows in the pulmonary circuit (Q_p) to systemic circuit (Q_s) is inversely proportional to the ratio of the pulmonary resistance (R_p) to the systemic resistance (R_s), i.e.

$$\frac{Q_p}{Q_s} \propto \frac{R_s}{R_p}$$

Pulmonary blood flow is also proportional to cardiac output (CO) so:

$$Q_p \propto (CO) \cdot Q_s \cdot \frac{R_s}{R_p}$$

Thus, any fall in the ratio R_s/R_p will cause a fall in pulmonary blood flow; for example, in pre-eclamptic toxæmia, the pulmonary vascular resistance increases and the cardiac output falls[37]. These factors would therefore decrease pulmonary blood flow, which could account for the observed deterioration in Eisenmenger's syndrome associated with hypertensive pregnancy[34].

What can be offered to the pregnant patient with Eisenmenger's syndrome? Unfortunately, abortion would appear to be the answer. The maternal mortality associated with abortion is only 7 per cent in comparison with 30 per cent for continuing pregnancy[35]. Because of the risk of thromboembolism, both systemic and pulmonary, we would suggest prophylactic anticoagulation with subcutaneous heparin. As in other cardiac cases, labour should not be induced unless there are good obstetric reasons. Induced labour carries a higher risk of Caesarian section, which is associated with a particularly high maternal mortality in Eisenmenger's syndrome[35].

Labour should be managed with careful epidural anaesthesia[35,38]. Although epidural anaesthesia could decrease the Q_p/Q_s ratio by decreasing the systemic vascular resistance, this does not seem to occur, at least when the anaesthetic is very carefully administered[39]. If the patient does become hypotensive, with increasing cyanosis and decreasing cardiac output, high inspired oxygen concentrations will decrease pulmonary vascular resistance, increase the Q_p/Q_s ratio and increase peripheral oxygen saturation[39]. In addition, alpha-sympathomimetic agents such as phenylephrine, methoxamine and noradrenaline will increase R_s and thus increase pulmonary blood flow[40]. Nevertheless, drugs such as tolazoline, phentolamine, nitroprusside and isoprenaline, which have been used to decrease pulmonary vascular resistance in other clinical situations, probably should not be given, since they will also decrease the systemic vascular resistance[40]. If the R_s decreases more than the R_p , pulmonary blood flow will decrease rather than increase. The same problem occurs with dopamine and beta-sympathomimetic drugs that have been given to increase cardiac output. They, too, will decrease R_s , and if R_s decreases more than the cardiac output increases, pulmonary blood flow will fall. The management of the deteriorating patient with Eisenmenger's syndrome therefore depends on giving oxygen and alpha-sympathomimetic amines.

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