Papers and Originals

Eisenmenger Syndrome in Pregnancy

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In 1897 Eisenmenger described the case of a 32-year-old man with a ventricular septal defect and an aorta overriding the right ventricle who had been cyanosed from infancy. Since then this combination of defects and symptoms has been known as the Eisenmenger complex. For over 50 years the overriding aorta was regarded as an essential feature of this complex and the cause of the cyanosis. Eisenmenger himself did not regard the dextroposition of the aorta as important in the physiological situation, and he was aware that a rise of pulmonary vascular resistance could equilibrate the pressures in the pulmonary and systemic circulations and so abolish the shunt and murmur. In the early 1950s it came to be recognized that the most characteristic feature of Eisenmenger's complex is the presence of severe pulmonary hypertension (Selzer and Laqueur, 1951). If a large ventricular septal defect is present the two ventricles act as one, discharging into both the pulmonary artery and the aorta; a sufficient distribution of blood to the systemic circulation is then possible only if the pulmonary vascular resistance approaches systemic levels.

Although this was realized in the early 1950s, it remained for Wood (1958) to point out that a similar haemodynamic situation occurs whenever a sufficiently large communication is present between the two sides of the heart, whether this occurs at ventricular, atrial, or aortopulmonary level. He listed twelve types of defect in which this haemodynamic situation can arise, and proposed the name Eisenmenger syndrome to describe this situation. He defined this as "pulmonary hypertension due to a high pulmonary vascular resistance with reversed or bidirectional shunt at aortopulmonary, ventricular, or atrial level." The clinical importance of Wood's work lies in the fact that it is easy to recognize clinically the haemodynamic situation by the signs of severe pulmonary hypertension with central cyanosis, but sometimes very difficult to recognize (even at catheterization) the site of the anatomical defect, for its characteristic murmur is not present and the volume of the shunt through the defect may be small. As a result of this work it is now usual to group together as the Eisenmenger syndrome certain cases of large ventricular septal defect, atrial septal defect, and patent ductus arteriosus, and these cases are clinically characterized by evidence of severe pulmonary hypertension and the presence of central cyanosis.

In a review of pregnant patients with congenital heart disease it was noticed that the maternal mortality was 27% (37 cases, 10 deaths) in cases classified as having the Eisenmenger syndrome, compared with 1.8% (837 cases, 15 deaths) in all other cases of shunts at aortopulmonary, atrial, and ventricular level reported since 1938, and the highest maternal mortality in any other type of congenital heart disease during the same period was 4.2% in Fallot's tetralogy (71 cases, three deaths) and 4.3% in coarctation of the aorta (232 cases, 10 deaths) (Table I). It therefore seemed worth while to study these cases in detail, especially as 16 cases of the

Eisenmenger syndrome (with 26 pregnancies) have been studied in our clinics, and only 21 other pregnant patients with the Eisenmenger syndrome have been reported.

TABLE I.—*Maternal Mortality in Various Types of Congenital Heart Disease in Cases Reported Since 1938*

Congenital Defect	No. of Cases Reported	No. of Deaths	Maternal Mortality (Percentage of Patients)
Patent ductus arteriosus	318	2	0.6
Atrial septal defect	261	5	1.9
Ventricular septal defect	187	5	2.7
Eisenmenger syndrome	37	10	27.0
Isolated pulmonary stenosis	122	0	0
Fallot's tetralogy	71	3	4.2
Coarctation of aorta	232	10	4.3
Complete atrioventricular block	42	0	0
Idiopathic dilatation of pulmonary artery	6	0	0
Ebstein's complex	8	0	0
	1,284	35	2.7

Methods

Since 1942 106 patients with congenital heart disease have attended the University Department of Cardiology, Manchester Royal Infirmary, during one or more pregnancies. In addition, 82 have attended at some time after pregnancy and in some cases also before pregnancy. The diagnoses in these patients are listed in Table II, together with the number of patients and

TABLE II.—*Congenital Heart Disease and Pregnancy: Personal Series*

Congenital Defect	Total No. of Patients	Total No. of Pregnancies	No. of Patients Observed During One or More Pregnancies	No. of Pregnancies Observed
Patent ductus arteriosus	36	64	18	24
Atrial septal defect	61	152	26	46
Ventricular septal defect	9	26	12	17
Eisenmenger syndrome*	16	26	12	13
Isolated pulmonary stenosis	29	69	19	27
Fallot's tetralogy	5	11	2	5
Coarctation of aorta	19	39	7	9
Disturbances of rhythm and conduction	7	17	7	12
Idiopathic dilatation of pulmonary artery	5	11	3	3
Ebstein's complex	1	1	0	0
Total	188	416	106	156

* Not included in other groups, even if site of defect known.

pregnancies observed; there were 26 pregnancies in 16 patients with the Eisenmenger syndrome, and 13 of these pregnancies were under our observation. After their first examination, which included an electrocardiogram and chest radiograph, patients were seen at monthly intervals until term. They were visited in St. Mary's Hospital over the period of delivery and assessed again three months post partum. Functional capacity was judged by symptoms graded according to the

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nomenclature adopted by the New York Heart Association (1964).

Cardiac catheterization was performed in 11 of the 16 patients with the Eisenmenger syndrome. The shunt was shown to be through a ventricular septal defect in seven of these, two of whom were also examined at necropsy. A patent ductus arteriosus was demonstrated clinically in three patients and at necropsy in a fourth. The site of the shunt was unknown in the remaining five patients, one of whom underwent cardiac catheterization. Coarctation of the aorta was present as an additional lesion in one patient.

Course of Pregnancy

There were five maternal deaths in the 16 patients with the Eisenmenger syndrome. This contrasts with the nil mortality in the 111 other patients with shunts; the only other maternal death in 416 pregnancies in our 188 cases of congenital heart disease was from rupture of the aorta in a patient with coarctation of the aorta.

Maternal Death in the Eisenmenger Syndrome

All five maternal deaths took place during labour or within the first seven days post partum.

Two patients, first seen at the 32nd and 34th weeks of pregnancy, were well and active until the 35th week of pregnancy; both then developed toxæmia, cyanosis increased, and one died in labour, the other four days post partum.

Case 1.—The patient had been cyanosed on exertion from early childhood, but was able to lead a normal active life. When seen at age 23 there were signs of pulmonary hypertension, with cyanosis and clubbing. When 25 she had a spontaneous abortion at three months, and the same year became pregnant again. Haemoptysis occurred at 26 weeks, but otherwise she remained well, and was first seen at 32 weeks, when the blood-pressure was 140/100 and the heart larger than two years previously. At 35 weeks she was admitted urgently to St. Mary's Hospital with albuminuria but no oedema; B.P. 140/105. The same day she went into labour, rapidly deteriorated, became grossly cyanosed and pulseless, and died undelivered. There was no necropsy.

Case 2.—The patient had no knowledge of heart disease, and was well and active prior to her first pregnancy at age 26. Some exertional dyspnoea occurred at 27 weeks. She was first seen at 34 weeks, when it was found that she had a pulmonary diastolic murmur and an accentuated pulmonary second sound. B.P. was 130/85 and the heart was slightly enlarged at fluoroscopy, with some intrinsic pulsation of the hilar vessels. A standard limb-lead electrocardiogram showed abnormal right axis deviation. At 35 weeks her dyspnoea suddenly increased, and by 37 weeks she was very ill with severe dyspnoea, orthopnoea, considerable dependent oedema, and slight cyanosis; B.P. was 150/110, and the urine contained albumin. The chest was clear, and the heart was not much enlarged (cardiothoracic ratio 0.52). She was admitted to St. Mary's Hospital. After 48 hours her condition was little changed, but the B.P. was 170–180/130; the membranes were ruptured artificially, and three hours later she was delivered by low forceps (birth weight, 4 lb. 4 oz.; 1,930 g.). Subsequently she improved, the albuminuria decreased, and the B.P. was in the range of 145/120 to 130/100. On the third post-partum day dyspnoea and cyanosis increased, and she had frequent attacks of severe cyanosis, although the chest remained clinically clear. She died on the fourth post-partum day, and at necropsy an aorto-pulmonary communication 2.5 cm. in circumference was found distal to the origin of the left subclavian artery; the pulmonary artery was much dilated and the right ventricular wall was 2.5 cm. thick (left ventricle 2 cm.).

The third death occurred suddenly and unexpectedly on the third post-partum day, presumably from ventricular arrest or cardiac standstill. There had been no sign of deterioration during pregnancy.

Case 3.—The patient had been breathless on exertion from early childhood. At age 24 she had signs of pulmonary hypertension,

central cyanosis, and finger-clubbing, and investigation established the presence of a ventricular septal defect with Eisenmenger syndrome; the heart was not enlarged (cardiothoracic ratio 0.45). At 27, when three months pregnant, her symptoms were of class II severity (New York Heart Association classification). At 32 weeks she had a slight haemoptysis, but her dyspnoea was unchanged and the heart was still not enlarged. Labour began at 36 weeks, and she lost about 1 pint (570 ml.) of blood before admission to St. Mary's Hospital. The first stage of labour lasted five and a quarter hours and the second 45 minutes; she was delivered without undue distress of a 4 lb. 4 oz. (1,930 g.) child, which survived. There was a post-partum blood loss of about 1 pint; haemoglobin was 101% on the day of delivery. Her condition remained satisfactory until the third post-partum day, when she suddenly collapsed with an impalpable pulse and extreme cyanosis. She was still breathing, but the heart sounds were inaudible and attempted resuscitation failed. At necropsy there was a ventricular septal defect 1 cm. in diameter, the pulmonary artery and all its branches showed severe atheroma, and the right ventricular wall was approximately the same thickness as that of the left ventricle. There were a few small areas of pulmonary collapse, but no signs of pulmonary embolism or thrombosis.

The other two deaths occurred after hysterotomy at 23 weeks and 30 weeks. Both patients developed syncopal attacks and increased cyanosis prior to operation.

Case 4.—The patient had been moderately disabled from early life, and at age 7 a diagnosis of ventricular septal defect with pulmonary hypertension was made at the London Hospital. From the age of 12 her disability increased so that she could walk only a few hundred yards or climb about six stairs without stopping. Before the age of 17 she had severe syncopal attacks with cyanosis, usually on exertion. At age 17 cardiac catheterization revealed a pulmonary arterial pressure of 121/77 (mean 94) mm. Hg, with a bidirectional shunt at ventricular level and an arterial oxygen saturation of 87%. Soon after this she became pregnant, and refused termination. At 18 weeks she had an attack of severe cyanosis and unconsciousness, from which she fully recovered in an hour. She was admitted to St. Mary's Hospital for rest at 26 weeks, and then had persistent tachycardia, rate 100–120/minute; B.P. 110/80. At 28 weeks, when in the lavatory, she had another attack of severe cyanosis and unconsciousness lasting 15 minutes; during this time her pulse was of good volume. Subsequently she remained more cyanosed, and complained of severe frontal headache. Two days later, when on a bedpan, she again lost consciousness; the heart rate rose to 180/minute, and she gradually recovered in half an hour, but remained intensely cyanosed and distressed by slight exertion in bed. There was no sign of peripheral or congestive heart failure, the chest was clear, and the heart was still not enlarged (cardiothoracic ratio 0.45). At 30 weeks there was no indication of the onset of labour, and it was decided to undertake caesarean section. A 2½-lb. (1,135-g.) child was delivered, and survived for two days. During induction of anaesthesia the cyanosis improved; heart rate and pulse were satisfactory throughout operation, but cardiac arrest occurred during skin-suturing and attempted resuscitation failed. Necropsy revealed a large ventricular septal defect, right ventricular enlargement, and pulmonary atheroma, but no sign of pulmonary embolism or thrombosis.

Case 5.—This patient was subjected to breathlessness, bronchitis, and frequent haemoptysis as a child (class II). At age 14 she was moderately cyanosed at rest, and cardiac catheterization revealed a bidirectional shunt through a ventricular septal defect; the pulmonary arterial pressure was 102/57 mm. Hg, and the arterial oxygen saturation was 81%. She was seen again at age 18, when she was 16 weeks pregnant, and her symptoms were unchanged. By 20 weeks she had become more fatigued (class III) and cyanosed, and there had been one syncopal attack. At 23 weeks pregnancy was terminated by hysterotomy; the child survived for 24 hours, and the operation was well tolerated, but the pulse rate was 120–140/minute post-operatively, and cyanosis persisted. On the fifth post-partum day she had several short attacks of mental confusion, and the next day, while sitting on a bedpan, she suddenly lost consciousness for five minutes and became intensely cyanosed; the heart rate was 130/minute and the B.P. 110/70. The cyanosis did not decrease for about 45 minutes. On the sixth post-partum day she had another attack of mental confusion, and that night she again lost consciousness and never recovered, although the heart remained regular while she was comatose. Necropsy was refused.

Course of 20 Pregnancies in 11 Surviving Patients

Six patients were in class I (no incapacity) before pregnancy ; two remained well during three pregnancies, but two of these pregnancies were terminated and the only full-term delivery was followed by exhaustion and two syncopal attacks five days post partum. Two of the other four patients developed symptoms during their only pregnancies, but produced living children ; one of these patients had a syncopal attack during pregnancy. The fifth patient had three spontaneous abortions, but gave birth to a living child in her fourth pregnancy and still remained well ; in her fifth pregnancy she developed moderate incapacity but again produced a living child. The sixth patient had some incapacity in her only pregnancy, and three days post partum she became very exhausted and cyanosed for two days, but the child survived. In this group 11 pregnancies gave six living children (Table III).

TABLE III.—Results of 26 Pregnancies in 16 Cases of the Eisenmenger Syndrome

Functional Class Before Pregnancy	Outcome	No. of Patients	No. of Pregnancies	Deterioration in Pregnancy	Living Child	Stillbirth (After 28 Weeks)	Spontaneous Abortion (Before 28 Weeks)	Therapeutic Abortion	Died Undelivered
I	Survived	6	11	4	6	0	3	2	0
	Died	2	3	—	1	0	1	0	1
II	Survived	5	9	1	3	2	3	1	0
	Died	3	3	—	2*	0	0	1†	0
Total		16	26	—	12	2	7	4	1

* One died after two days. † At 23 weeks ; child survived 24 hours.

Five patients were in class II (slight incapacity) prior to pregnancy and four did not deteriorate in six pregnancies, but three pregnancies ended in spontaneous abortion, one was terminated, and the other two led to stillbirths. Only one patient in class II prior to pregnancy had living children ; she had three, but in the third pregnancy she developed severe symptoms (class III). Thus, nine pregnancies in this group produced three living children, all in the one patient (Table III).

Results of Pregnancy

In a total of 26 pregnancies with five maternal deaths, only 12 children were born alive ; nine of these were premature and one died after two days. Two children survived, although the mothers died. Two mothers produced five of the 11 children who survived. One child was born with the Eisenmenger syndrome. The average birth-weight of the eight infants in whom this was recorded was 4 lb. 11 oz. (2,125 g.), including the two full-term infants (average birth weight 6 lb. 15 oz. ; 3,120 g.).

Of eight patients who were free from symptoms before pregnancy two died owing to pregnancy, and of eight with class II incapacity before pregnancy three died. Capacity for effort before pregnancy is not a reliable indication of the danger of pregnancy in these cases, though both of the asymptomatic patients who died developed toxæmia of pregnancy. Fourteen pregnancies in class I patients produced seven living children, and 12 pregnancies in class II patients gave five living children, of whom one died after two days (Table III). Of 11 patients who had spontaneous or therapeutic abortions only one (Case 5) died in that pregnancy (at 23 weeks).

Review of Previously Reported Cases

On reviewing the literature on congenital heart disease and pregnancy it is sometimes difficult in the earlier reports to be certain of the exact nature of the cardiac lesion ; after careful

scrutiny, however, it has been possible to collect reports of pregnancy in 21 patients (with five deaths) in which a diagnosis of the Eisenmenger syndrome seemed established ; this was confirmed at catheterization or necropsy in 18 instances. The authors, sites of the shunts, and number of cases each has reported are listed in Table IV. Until the work of Wood (1958) these cases (all with severe pulmonary hypertension, but with shunts at differing levels) had not been regarded as a clinical and haemodynamic group ; consequently, no author has previously reviewed them as a single group in relation to pregnancy.

TABLE IV.—Pregnancy in 21 Reported Cases of the Eisenmenger Syndrome

Author	Site of Shunt or Type of Lesion	No. of Cases
Lund (1948)	P.D.A.	1
Carter (1948)	Unknown	1
Lindeboom (1948)	V.S.D.	1
Simon and Lustberg (1951)	Truncus arteriosus	1
Poincarret (1954)	Unknown	1
Laake (1954)	Unknown	1
Campbell (1955)	P.D.A.	1
Burwell and Metcalfe (1958)	P.D.A. (1). Unknown (1)	2
Mendelson (1960)	V.S.D.	1
Jacobi <i>et al.</i> (1961)	Unknown (2)	2
Jewett (1961)	V.S.D. (1). ?A.S.D. (1)	2
Buermann and Kragelund (1962)	P.D.A., A.S.D., and V.S.D.	1
Lyon <i>et al.</i> (1962)	P.D.A.	1
Penman and Whitty (1963)	Cor triloculare biatriatum	1
Zeh and Klaus (1963)	V.S.D. (2). A.S.D. (1). Unknown (1)	4

Death occurred after delivery in all five fatal cases. All were examined at necropsy, but the immediate cause of death was uncertain in all these cases. In four cases, however, the modes of death appear to be similar to those in our cases.

In one case (Lund, 1948) a 26-year-old patient developed toxæmia at 24 weeks, the blood-pressure was 200/120, and she died 30 minutes after caesarean section under local anaesthesia (cf. Cases 1 and 2).

Two patients died unexpectedly (cf. Case 3). Buermann and Kragelund's (1962) 32-year-old patient developed dyspnoea and palpitation in her third pregnancy, and changed from functional class II to III. During delivery at 36 weeks she became more cyanosed but was otherwise well ; she died suddenly at home on the eleventh post-partum day ; presumably from ventricular fibrillation or standstill. Simon and Lustberg's (1951) 19-year-old primipara with a truncus arteriosus had some cyanosis and dyspnoea but was otherwise well until the third post-partum day, when headache and tachycardia were followed by a voluminous bowel movement, collapse, and death. It was believed that she died from pulmonary infarction, but there is no record of necropsy confirmation.

One patient (Jewett, 1961) died after attacks of syncope and cyanosis (cf. Cases 4 and 5). She was well when first seen at the age of 18, 23 weeks on in her first pregnancy. At 33 weeks she developed abruptio placentae, was delivered and transfused, and her condition was satisfactory. On the fifth post-partum day she had repeated attacks of cyanosis and syncope, and the next day complained of headache, suddenly became cyanosed and comatose, and died within a few minutes.

The fifth death was reported by Lindeboom (1948). A 33-year-old patient developed oedema and dyspnoea and increased cyanosis at the 36th week of her second pregnancy (one previous spontaneous abortion). Induced labour was followed by the birth of a normal infant, but on the fifth post-partum day dysarthria and neurological signs developed, and death was attributed to cerebral thrombosis or a paradoxical embolus, but this could not be established at necropsy.

These five deaths in 21 recorded cases, together with the five deaths in our 16 patients, give a combined mortality of 27%—far greater than in any other type of congenital heart disease ; since 1938 the highest mortality in other groups is 4.2% in Fallot's tetralogy and 4.3% in coarctation of the aorta (Table I).

Of the 16 non-fatal cases previously reported the cardiac state apparently did not deteriorate in nine cases (Carter, 1948; Laake, 1954; Campbell, 1955; Jacobi *et al.*, 1961; Jewett, 1961; Zeh and Klaus, 1963). Of the remaining seven patients four developed increased cyanosis during pregnancy (Burwell and Metcalfe, 1958; Mendelson, 1960; Jacobi *et al.*, 1961; Penman and Whitty, 1963), usually in the last few weeks before delivery. Four patients became more breathless (Poincarret, 1954; Burwell and Metcalfe, 1958, two cases; Penman and Whitty, 1963); Poincarret's patient developed heart failure during pregnancy, and in Penman and Whitty's case failure occurred eight days post partum. Two patients developed toxæmia (Campbell, 1955; Lyon *et al.*, 1962). Apart from toxæmia the patient of Lyon *et al.* was well until the fourth post-partum day, when the blood-pressure again increased and she developed moderate dyspnoea and orthopnoea with episodes of cyanosis which persisted for a week. She recovered and was discharged 23 days post partum; over the next few days these symptoms subsided and the blood-pressure returned to normal.

In reported cases only partial information is available concerning the outcome of pregnancy, and in two cases there is no information. In 18 of the remaining 19 cases, 27 pregnancies were mentioned, with 16 living children, of whom eight are recorded as delivered prematurely and two at full term. Among the 11 unsuccessful pregnancies were eight spontaneous and two therapeutic abortions, and one child died after premature delivery. The remaining patient (Zeh and Klaus, 1963) is exceptional, for she was first investigated at age 51, after nine pregnancies, of which eight apparently went to term. The haemodynamic situation was not known during the pregnancies.

Discussion

In large ventricular and aortopulmonary defects the size and direction of the shunt depend upon the relative resistances to flow in the pulmonary and systemic circuits. In the Eisenmenger syndrome pulmonary and systemic resistances are approximately equal and the shunt is almost balanced. A sudden increase in right-to-left shunting, associated clinically with increased cyanosis, can occur in one of two ways—either owing to a sudden rise of pulmonary vascular resistance or to a sudden fall of systemic resistance. From the case histories previously described it seems clear that in the Eisenmenger syndrome such changes in vascular resistance usually occur either late in pregnancy or, more often, in the immediate post-partum period.

Of all the conditions in which the systemic vascular resistance may suddenly fall late in pregnancy or soon after delivery, toxæmia seems the most obvious. Lund (1948) observed that when systemic hypertension (usually due to toxæmia) occurred in patients with a shunt it reached a peak at about the time of delivery. A few minutes after delivery the blood-pressure dropped suddenly, cyanosis increased, shock developed, and one patient died. It is interesting to compare the situation in Fallot's tetralogy with that in the Eisenmenger syndrome. Both are associated with systemic pressures in the right ventricle and with a balanced or bidirectional shunt, but the obstruction to outflow to the lungs is at or near the pulmonary valve in Fallot's tetralogy, whereas it is in the pulmonary vasculature in the Eisenmenger syndrome. Among 71 reported cases of pregnancy in Fallot's tetralogy there were only three deaths, and two of these were associated with toxæmia. In normal pregnancy changes in systemic and pulmonary vascular resistance occur in parallel, but in Fallot's tetralogy the resistance to outflow from the right ventricle can vary little, for it is due to pulmonary stenosis; consequently if the systemic resistance falls increased right-to-left shunting will follow. There is reason to believe that in the Eisenmenger syndrome it is very difficult to lower the high pulmonary vascular resistance; for instance, it does not fall with infusion of

acetylcholine or on breathing 100% oxygen, and it is probable that it cannot fall in parallel with the systemic resistance in pregnancy, as it does in normal pregnancy. Consequently, as in Fallot's tetralogy, a sudden fall in systemic blood-pressure will lead to increased right-to-left shunting and a fall of pulmonary blood-flow.

Although toxæmia is a dangerous complication both in the Eisenmenger syndrome and in Fallot's tetralogy, the maternal mortality is much higher in the Eisenmenger syndrome (27%) than in Fallot's tetralogy (4.2%), and the increased mortality in the Eisenmenger syndrome is not due to an increased incidence of toxæmia. The only condition with a comparable mortality in pregnancy is primary pulmonary hypertension, and it is probably significant that one important haemodynamic difference between the Eisenmenger syndrome and Fallot's tetralogy is the presence of pulmonary hypertension at systemic levels in the former. Severe pulmonary hypertension is undoubtedly itself a most dangerous condition in pregnancy; the mother died in eight of 15 reported cases (Dressler, 1952; Whittemore *et al.*, 1956; Chapman *et al.*, 1957; Evans *et al.*, 1957, two cases; Kuida *et al.*, 1957; Burwell and Metcalfe, 1958; Etheridge, 1958; Rosen *et al.*, 1959; Jewett, 1961, three cases; Nielsen and Fabricius, 1961; Zeh and Klaus, 1963). The modes of death were very similar to those in the Eisenmenger syndrome. All eight patients died suddenly: two died undelivered (in mid-pregnancy and at 31 weeks); one died during labour; three died immediately after delivery (termination at 22 weeks, caesarean section at eight months, and following forceps delivery); and two died post partum, one shortly after delivery and one 14 days post partum. Repeated syncopal attacks during pregnancy are recorded in six cases, and four of these patients died. Cyanosis is recorded in four cases, with three deaths. Clinical details are inadequate in some of these cases, but one of the better-reported cases (Jewett, 1961, Case 1) illustrates the similarity to our Cases 4 and 5.

A 23-year-old primipara had been well before pregnancy, and remained well during pregnancy, apart from slight albuminuria in the last four weeks. After a normal delivery she was well until the fifth post-partum day, when she had a syncopal attack which was followed by tachycardia lasting some hours. The following day, while using a bedpan, she had a severe syncopal attack, which was erroneously attributed to massive bleeding. From that time attacks of intense distress with dyspnoea, cyanosis, and tachycardia occurred, sometimes on slight activity in bed but also apart from exertion. She had improved somewhat by the 13th post-partum day, but the next morning she awoke severely dyspnoeic and cyanosed, and died an hour later. There were necropsy findings indicating long-standing pulmonary hypertension.

In our Cases 4 and 5 the pregnancy was terminated surgically at 30 and 23 weeks on account of the severe symptoms. It is probable that, as in other critical situations in pregnancy, the patient's chances of survival are never increased by surgical intervention late in pregnancy. The liability to death soon after intervention late in pregnancy may be merely a reflection of the desperate clinical state of these patients at the time. Termination of pregnancy before 20 weeks in patients who have not deteriorated is a comparatively safe procedure and gave no trouble in three of our cases.

The maternal mortality of 53% in primary pulmonary hypertension is even higher than the 27% maternal deaths in the Eisenmenger syndrome. There are two possible reasons for this difference: either the shunt acts in some way as a safety-valve when the right ventricle is working against a critically high resistance, or the progressive character of primary pulmonary hypertension imposes an additional hazard. Comparison of these two conditions suggests that it is unlikely that, when the pulmonary vascular resistance increases, the consequent increased right-to-left shunting is itself dangerous to the mother (though it may be to the child), but the increased cyanosis will, of course, be a clinical indication of a sudden rise of pulmonary vascular resistance, provided the

systemic blood-pressure is maintained. This was the case in three of our patients who had attacks of unconsciousness and cyanosis in which the systemic blood-pressure and peripheral pulses remained good.

In considering the possible ways in which a sudden rise of pulmonary vascular resistance may occur in these conditions it is interesting to note that in recorded cases in which sudden deterioration with increased cyanosis occurred in the post-partum period, pulmonary embolism was nearly always suspected clinically, but in none of these cases was there necropsy evidence of either appreciable pulmonary infarction or of peripheral thrombophlebitis. Although massive pulmonary embolism has been excluded as a cause of increased obstruction to right ventricular outflow in these cases, it is much more difficult to exclude at necropsy the possibility that small post-partum pulmonary emboli triggered off widespread pulmonary vasoconstriction.

There is no doubt that the puerperium is a dangerous period in many types of heart disease; in mitral stenosis a high proportion of deaths from pulmonary oedema occur at this time (Morgan Jones, 1959). Five of the eight reported deaths in primary pulmonary hypertension occurred within two weeks after delivery, and Hamilton and Thomson (1941) found that 75% of the deaths in their cases of heart disease occurred during the puerperium. Of the 11 deaths in the Eisenmenger syndrome seven occurred between the third and eleventh post-partum days and the other four during or immediately after spontaneous or artificial delivery. The haemodynamic factors leading to death at this time are still little understood. In a minority of these cases the association with delivery and the early puerperium may be fortuitous; thus the uterus was evacuated or hysterotomy performed owing to the grave condition of the patient in four of the eleven deaths in the Eisenmenger syndrome and in three of the eight deaths in primary pulmonary hypertension. In these cases death following artificial delivery may have been due more to the grave condition of the patients than to the termination of pregnancy or the subsequent post-partum haemodynamic changes.

In eight of our 16 cases there was no appreciable incapacity before pregnancy, yet two of these patients died owing to pregnancy. The functional capacity before pregnancy is not a good guide to the danger of pregnancy in these cases; indeed, the mortality in those who were fit before pregnancy (two out of eight) was not significantly different from the mortality in patients with incapacity prior to pregnancy (three out of eight), though the numbers of available cases are much too small to establish this point.

Summary

The Eisenmenger syndrome is a haemodynamic situation in which pulmonary hypertension at systemic levels is associated with a reversed or bidirectional shunt at atrial, ventricular, or aortopulmonary level. This haemodynamic situation can be readily recognized clinically by the combination of central cyanosis with obvious signs of pulmonary hypertension, but the site of the defect is much more difficult to locate, even at catheterization.

The effects of pregnancy have not previously been studied in the whole group of patients with this haemodynamic picture. Sixteen personal cases with 26 pregnancies are compared with

21 cases collected from the literature. The maternal mortality is much higher (27%) than in any other group of patients with congenital cardiac lesions, the highest comparable mortality being 4.3% in coarctation of the aorta and 4.2% in Fallot's tetralogy. It is suggested that the degree of pulmonary hypertension is the most important factor in the mortality, and an even higher maternal mortality has been recorded in primary pulmonary hypertension (53%). The modes of death are essentially similar in the two conditions, usually following syncopal attacks or circulatory collapse. Death commonly occurs about the time of delivery or during the puerperium. Even patients asymptomatic before pregnancy are at considerable risk during pregnancy and in the puerperium.

The possible mechanisms of death are discussed, and the possibility that a sudden rise in the pulmonary or fall in the systemic vascular resistance may lead to fatal haemodynamic disturbances is considered. Toxaemia of pregnancy is sometimes an important contributory factor, perhaps because it may be associated with sudden changes of peripheral vascular resistance. Interference with the pregnancy after 20 weeks has proved dangerous, but termination before 20 weeks has been carried out without complications. Premature delivery and spontaneous abortion are common, and the child survived in only 12 of 26 pregnancies.

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