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ATRIAL FIBRILLATION AND PREGNANCY

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Atrial fibrillation occurring in the child-bearing age is most commonly associated with rheumatic heart disease. Its onset usually signifies an advanced stage in the natural course of the underlying cardiac condition, and therefore patients with atrial fibrillation complicating rheumatic heart disease have often been advised not to become pregnant or, if pregnant, to have the pregnancy terminated (MacRae, 1955). On the other hand, Morgan Jones (1951) expressed the view that one should not be unduly intimidated by the mere presence of atrial fibrillation and that the capacity for effort is a more important prognostic feature. Bramwell (1953) also stated that although atrial fibrillation adds to the risks of pregnancy it should not be regarded as a contra-indication to it provided the patient can be kept under adequate supervision.

Atrial fibrillation is a frequent precursor of heart failure, and as such it is an important factor in assessing the risks of pregnancy (Gilchrist and Haig, 1950; Bramwell, 1953). It is the purpose of this paper to evaluate the immediate risks and the remote effects of pregnancy in patients with rheumatic heart disease and atrial fibrillation.

Material.—Among 760 consecutive pregnancies in 550 patients with rheumatic heart disease studied between 1942 and 1959 there were 60 pregnancies in 50 patients which were complicated by transient or permanent atrial fibrillation. Among the pregnant women with known heart disease, other than rheumatic, studied during the same period, we were unable to find a single instance of atrial fibrillation.

Clinical Findings

The 50 patients in the atrial fibrillation group were between 18 and 44 years of age, the average age being 30.

The onset of atrial fibrillation in relation to the 60 pregnancies is shown in Table I. In 31 instances it was either known with certainty or assumed on reasonable grounds that atrial fibrillation had been present before pregnancy, and in 29 instances the ectopic rhythm appeared during pregnancy or in the puerperium. Three patients with permanent atrial fibrillation experienced previous paroxysms of fibrillation. Two patients with paroxysmal and four patients with permanent atrial fibrillation also had previous paroxysms of supraventricular tachycardia.

TABLE I.—*Onset of Atrial Fibrillation in Relation to 60 Pregnancies Complicated by Rheumatic Heart Disease*

Atrial Fibrillation	Before Pregnancy	During Pregnancy	In Puerperium
Transient	—	5	1
Permanent ..	31	14	9

Valvular Lesion.—Twenty-seven patients had pure mitral stenosis and six had significant mitral incompetence as well. The remaining 17 showed signs of both mitral and aortic valve disease, significant aortic stenosis being present in only one case.

Cardiac Enlargement.—For the purposes of this study cardiac enlargement was graded as slight (cardiothoracic ratio less than 55%), moderate (c.t.r. 55–60%), and considerable (c.t.r. over 60%). When no teleradiograph was available a similar grading was attempted, based on the impression gained from radioscopic examination. Accordingly, 11 patients were regarded as having slight, 32 patients moderate, and 7 patients considerable cardiac enlargement.

Electrocardiogram.—When first examined during pregnancy, 13 patients had right ventricular hypertrophy, 14 had left ventricular hypertrophy, and 4 showed a biventricular strain pattern; in 12 patients the QRS complexes conformed to a normal pattern. In the remaining seven the chest leads were inadequate for a detailed study. Significant variation in the ventricular complex took place during pregnancy in three patients: in two from a normal pattern to right ventricular hypertrophy and to left ventricular hypertrophy, respectively; and in one patient from right ventricular hypertrophy to left ventricular hypertrophy, but this change occurred after mitral valvotomy.

Heart Failure.—Seventeen pregnancies were complicated by pulmonary congestion and three by frank pulmonary oedema. Right heart failure occurred in nine pregnancies. The incidence of heart failure in relation to the onset of atrial fibrillation is shown in Table II, which also includes comparative figures for the sinus rhythm group. When atrial fibrillation had been present before pregnancy, heart failure occurred either during pregnancy or in the puerperium in 25.8% of the cases. When the change from sinus rhythm to atrial fibrillation took place during pregnancy or in the puerperium, heart failure developed in 72.4% of the cases. In this latter group heart failure developed in 10 patients while still in sinus rhythm, in three with the onset of atrial fibrillation, and in one patient during an attack of paroxysmal tachycardia; in the remaining seven patients heart failure appeared between one week and six months after the onset of atrial fibrillation. The three episodes of acute pulmonary oedema occurred during an attack of paroxysmal tachycardia, four months after the onset

TABLE II.—*Incidence of Heart Failure in Relation to Cardiac Rhythm in 760 Pregnancies Complicated by Rheumatic Heart Disease*

Cardiac Rhythm	No. of Pregnancies	Heart Failure		
		Pulmonary Congestion	Acute Pulmonary Oedema	Right Heart Failure
Sinus rhythm group	700	153	12	11
Atrial fibrillation group: Onset before pregnancy	31	4	1	3
Atrial fibrillation group: Onset during pregnancy or in puerperium	29	13	2	6
Total	760	170	15	20

of atrial fibrillation, and after long-established atrial fibrillation, respectively. Three patients who developed permanent atrial fibrillation and also heart failure in their first, second, and fifth pregnancy, respectively, had no heart failure in a subsequent pregnancy, but the last patient underwent mitral-valve surgery before her sixth pregnancy. The incidence of heart failure in relation to the degree of cardiac enlargement is shown in Table III, and in relation to age in Table IV.

TABLE III.—*Incidence of Heart Failure in Relation to Cardiac Enlargement in 60 Pregnancies Complicated by Rheumatic Heart Disease and Atrial Fibrillation*

Cardiac Enlargement	No. of Pregnancies	Heart Failure
Slight (c.t.r. <55%)	13	38·5%
Moderate (c.t.r. 55–60%)	39	48·7%
Considerable (c.t.r. >60%)	8	62·5%

TABLE IV.—*Incidence of Heart Failure in Relation to Age in 60 Pregnancies Complicated by Rheumatic Heart Disease and Atrial Fibrillation*

Age	No. of Pregnancies	Heart Failure
18–19	3	0
20–29	28	35·7%
30–39	26	61·5%
40–44	3	100%

Embolism.—Arterial embolism occurred in six patients. In one patient it appeared during a paroxysm of atrial fibrillation. In three patients it appeared 24 hours, eight days, and nine days, respectively, after the onset of established atrial fibrillation. In the fifth patient it occurred during an episode of atrial tachycardia, seven days after the first recognized paroxysm of atrial fibrillation; four months later she developed permanent atrial fibrillation. In the sixth patient atrial fibrillation had already been present before pregnancy.

Pulmonary embolism was suspected in 11 patients, four of whom also had arterial emboli. In one patient pulmonary embolism followed termination of pregnancy, and in another patient delivery by caesarean section. One episode of pulmonary embolism was fatal. The incidence of embolism in relation to cardiac rhythm is shown in Table V.

TABLE V.—*Incidence of Embolic Episodes in Relation to Cardiac Rhythm in 760 Pregnancies Complicated by Rheumatic Heart Disease*

Cardiac Rhythm	No. of Pregnancies	Embolism		
		Pulmonary	Limb	Cerebral
Sinus rhythm	700	6	0	5
Transient or established atrial fibrillation	60	11	5	1

Mitral Valvotomy.—Six patients developed atrial fibrillation after mitral valvotomy carried out at various stages of pregnancy. In four of these sinus rhythm was restored with procainamide or quinidine, and the condition of these four had been satisfactory during the remainder of pregnancy. In one patient we did not succeed in restoring normal rhythm, and in another no attempt was made at conversion. Anticoagulant prophylaxis was used in one patient. The two patients who remained in atrial fibrillation developed progressive cardiac enlargement during pregnancy, and one of them also had right heart failure in the puerperium. Two further patients included in the present analysis underwent mitral-valve surgery during pregnancy and in the puerperium, respectively. One of these already had established atrial fibrillation before her first pregnancy. She had no signs of heart failure, but she was advised to undergo cardiac surgery at this stage because of marked pulmonary hypertension and electrocardiographic evidence of severe right ventricular hypertrophy. Her post-operative course had been smooth and she also had three further uneventful pregnancies. The other patient developed permanent atrial fibrillation during her fifth pregnancy. She had an attack of acute pulmonary oedema in the puerperium, after which she underwent mitral-valve surgery. A subsequent pregnancy, her sixth, was uneventful. In all, atrial fibrillation complicated seven pregnancies observed after mitral valvotomy. In all seven instances the arrhythmia had developed before the pregnancy in question, and in five it had already been present prior to valvotomy. The four above-mentioned pregnancies and a fifth one were uneventful, one was complicated by haemoptysis without heart failure, and there was one miscarriage in the absence of heart failure.

Maternal Mortality.—Three patients died in this series. A 29-year-old woman with mitral-valve and aortic-valve disease and moderate cardiac enlargement died in the ninth month of her first pregnancy from progressive right heart failure, four months after the onset of atrial fibrillation. A 24-year-old primipara with pure mitral stenosis died suddenly, presumably from pulmonary embolism, 13 days after delivery, 11 days after the onset of atrial fibrillation, and three days after an episode of popliteal embolism. A 21-year-old primipara who developed atrial fibrillation during pregnancy also died suddenly on the 22nd day after delivery. Post-mortem examination showed a tight mitral stenosis and obstruction of the tricuspid orifice by a large mobile tumour-like structure which proved to be an aneurysm of the atrial septum filled with blood clots.

Mode of Delivery and Foetal Mortality.—Fifty-three pregnancies were dealt with by the vaginal route, and in 16 of these prophylactic forceps was applied. Caesarean section was carried out in three patients, in two of them for clear obstetric reasons. The total foetal loss amounted to 12, including four neonatal deaths. One patient died undelivered. One pregnancy was terminated, and there were two miscarriages. There were four stillbirths, three of which were due to prematurity. The high incidence of prematurity was a striking feature in this series, 20 pregnancies terminating before 38 weeks.

Subsequent Course.—Seven patients died between 2 and 11 years after their last pregnancy. Two patients who had pulmonary congestion during pregnancy died two years after delivery from right heart failure. One patient who had an attack of acute pulmonary oedema while pregnant died two and a half years later after mitral valvotomy. One patient with right heart failure during pregnancy died seven years later from recurrent heart failure. Three patients who had no heart failure

during pregnancy died 3, 8, and 11 years later from pulmonary embolism, from progressive right heart failure, and after mitral valvotomy, respectively. Seventeen other patients had deteriorated between 2 and 10 years after pregnancy. Nine of these underwent mitral valvotomy, and all nine have since improved. Ten of these 17 patients experienced heart failure during pregnancy. Twenty-three patients, including six who had only transient atrial fibrillation and are now still in sinus rhythm, and one woman who miscarried, have shown no signs of deterioration since their last pregnancy over a period of observation averaging six years (1 to 16 years). Fourteen of these patients showed signs of heart failure during pregnancy. Ten patients in this group underwent mitral-valve surgery either before or during pregnancy.

Discussion

Out of 760 consecutive pregnancies in 550 patients with rheumatic heart disease 60 were complicated by paroxysmal or established atrial fibrillation. In 29 instances the arrhythmia started during pregnancy or in the puerperium. Thus atrial fibrillation developed in about 4% of the pregnancies which started in sinus rhythm.

In a previous study (Szekely and Snaith, 1953) we drew attention to an increased susceptibility to paroxysmal atrial tachycardia in pregnancy, and the question arises whether this also applies to atrial fibrillation. Burwell and Metcalfe (1958) suggested that the increased blood volume in pregnancy may precipitate atrial fibrillation in mitral stenosis owing to further distension of the left atrium. Wood (1954) also stated that atrial dilatation can cause atrial fibrillation. The tendency to develop atrial fibrillation after mitral-valve surgery is well recognized, and it may be of interest that in a personal series of 95 patients with sinus rhythm subjected to mitral valvotomy the incidence of post-operative atrial fibrillation was 40% when the operation was carried out during pregnancy (15 cases), and only 21% when it was done in the non-pregnant state (80 cases). This difference may be even more significant if one considers that those who were operated on in the non-pregnant state were as a group in a more advanced stage of the disease. The data of Mendelson (1955) also show a relatively high incidence of atrial fibrillation after mitral valvotomy carried out during pregnancy.

Many of our patients had been receiving digitalis for varying periods prior to the onset of atrial fibrillation. However, an analysis of all the relevant data failed to give a clear indication of how far digitalis could be held responsible, if at all, for the development of atrial fibrillation.

The significance of atrial fibrillation in relation to pregnancy in the presence of rheumatic heart disease lies in the fact that by comparison with the sinus-rhythm group it carries a greater risk of heart failure and embolism, resulting in a higher maternal mortality rate and foetal loss (Table VI). These complications are attributable partly to the atrial fibrillation itself and partly to the severity of the underlying cardiac condition (Fraser and Turner, 1955).

The relative frequency and prognosis of acute pulmonary oedema and right heart failure in pregnant women with heart disease was discussed by Morgan Jones (1959). He found in an unselected group of patients that pulmonary oedema occurred less than half as frequently as right heart failure but carried a graver immediate prognosis. Our experience is in keeping with this opinion regarding the immediate prognosis. However, the difference in the frequency of the two types of heart failure in our material was obvious only in the small atrial fibrillation group (Table II). We believe that on the whole we have been more successful in preventing right heart failure than acute pulmonary oedema.

TABLE VI.—*Maternal and Foetal Mortality in 760 Pregnancies Complicated by Rheumatic Heart Disease*

Cardiac Rhythm	No. of Pregnancies	Maternal Deaths						Foetal Loss %
		Heart Failure	Embolism	Active Rheumatic Carditis	Circulatory Obstruction from Atrial Aneurysm	Non-cardiovascular	Total %	
Sinus rhythm ..	700	5	0	1	0	1	1	8·5
Atrial fibrillation	60	1	1	0	1	0	5	20
Total ..	760	6	1	1	1	1	1·3	9

The incidence of heart failure in the atrial fibrillation group as a whole showed a direct relationship to the degree of cardiac enlargement and to increasing age. However, when the cases were considered in two separate groups—namely, those in which atrial fibrillation had already been present before pregnancy and those in which the ectopic rhythm developed during pregnancy—the most striking feature was the significantly higher incidence of heart failure in the latter group.

Arterial embolism in rheumatic heart disease is said to occur more often in the presence of atrial fibrillation than in sinus rhythm, and our findings support this view. Our observations also show, in accordance with those of Wood (1956) and Riss and Levine (1958), that there is a definite tendency to embolization shortly after the onset of atrial fibrillation.

The present observations show that atrial fibrillation complicating rheumatic heart disease is an added risk to the pregnant woman. However, the introduction of a system of management aiming at the prevention of heart failure (Gorenberg, 1943; Snaith and Szekely, 1951; Gorenberg and Chesley, 1958) and the more recent therapeutic advances have greatly reduced the risks. Our three maternal deaths, two of which could be regarded to-day as potentially preventable, occurred in the first series between 1942 and 1949 (Snaith and Szekely, 1951), and since 1950 we have had no fatality in 39 pregnancies complicated by atrial fibrillation. The onset of atrial fibrillation in rheumatic heart disease should be regarded as a medical emergency (Wood, 1956), and we now believe that in suitable cases every effort should be made to restore sinus rhythm should spontaneous or post-valvotomy atrial fibrillation appear during pregnancy or in the puerperium. After adequate digitalization the administration of quinidine or procainamide during pregnancy carries no added risks, and judicious anticoagulant prophylaxis can also be made a safe procedure (Mendelson, 1956; Burwell and Metcalfe, 1958).

If restoration of sinus rhythm is not achieved the advisability of long-term anticoagulant therapy should be considered. Mendelson (1956) recorded a 23% incidence of embolism in pregnancy complicated by atrial fibrillation, and he advocates anticoagulant prophylaxis unless specific contraindications exist. Once labour has started, anticoagulants should be temporarily withheld and vitamin K can be administered. Mendelson (1956) advises that vitamin K should also be given to the infant

and that breast-feeding should not be allowed. The choice of the anticoagulant drug is also to be considered. In a recent case of cerebral embolism occurring two weeks prior to term we used only heparin ; the patient fully recovered, and heparin produced no ill effects in the mother or baby. Obviously, much wider clinical experience is needed in this particular field.

The many variable factors, including mitral-valve surgery in several patients before or during pregnancy, made an assessment of the remote effects of pregnancy on the course of the heart disease rather difficult. Furthermore, Rowe *et al.* (1960) suggested that medically treated patients with mitral stenosis probably live longer now than they did ten or twenty years ago. Nevertheless, consideration of data reported in the literature (Olesen, 1955 ; Wood, 1956 ; Rowe *et al.*, 1960) and our own observations relating to the natural history of rheumatic heart disease have led us to believe that pregnancy, if appropriately managed and survived, does not accelerate the course of rheumatic heart disease, save perhaps in exceptional cases. This is also the view of several other workers (Miller and Metcalfe, 1956 ; Burwell, 1958 ; Gorenberg and Chesley, 1958).

Summary

The course of 60 pregnancies complicated by rheumatic heart disease and paroxysmal or established atrial fibrillation is analysed, and some of the features are compared with those observed in 700 pregnancies with rheumatic heart disease in which sinus rhythm had been maintained throughout pregnancy and the puerperium.

The incidence of heart failure and embolic episodes was higher in the atrial fibrillation group, resulting in a higher maternal mortality rate and foetal loss. However, improved methods in the care of the pregnant patient with functionally severe heart disease have considerably reduced these risks.

The belief is expressed that if atrial fibrillation appears during pregnancy or in the puerperium an attempt should be made to restore sinus rhythm. Anticoagulant prophylaxis, if judged advisable, is also feasible during pregnancy.

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VIRUS EXCRETION AFTER MASS VACCINATION WITH ATTENUATED POLIOVIRUSES IN HUNGARY

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Hungary experienced her most extensive poliomyelitis epidemics in the years 1957 and 1959 (Rudnai, 1958, 1960). Both were caused by the type 1 poliovirus (Molnár, 1958 ; Földes *et al.*, 1959 ; Mécs *et al.*, 1961 ; Dömök and Molnár, 1961). The 1959 epidemic provided evidence that poliomyelitis epidemics might be moderated but not prevented by the wide-scale use of the Salk vaccine (Bakács, 1960 ; Rudnai, 1961). The excellent results of the oral vaccination with the Sabin strains in the U.S.S.R. (Chumakov *et al.*, 1959) induced Hungary to organize nation-wide vaccination with the same vaccine. During November 3–5, 1959, children from 3 months to 15 years of age were eligible in one county (Györ-Sopron county) for feeding trivalent vaccine containing 100,000 CPD50 of each type per dose. The same children were revaccinated with the same dose of trivalent vaccine during December 17–19, 1959. The average acceptance rate was 96%. Subsequently the children of the same age-groups were eligible for vaccination in the whole country, except for Györ-Sopron county. In this case the single types were fed separately in the following periods: type 1, December 14–19, 1959 ; type 3, January 21–27, 1960 ; type 2, February 23–27, 1960. The average acceptance rate was 92.4% (Kátay, 1961).

Virus excretion was studied in connexion with both campaigns. We wished to obtain data (1) on prevaccination excretion of enteroviruses ; (2) on postvaccination excretion by age of the Sabin strains ; (3) on the relative effectiveness of simultaneous feeding ; (4) on the effectiveness of refeeding the trivalent vaccine : and (5) on the interactions between wild enteroviruses and the vaccine strains, and among the vaccine strains. The reproductive capacity at 40° C. (Sabin, 1961) of the strains excreted by healthy subjects on the days preceding vaccination and of those reisolated from healthy vaccinees was also studied.

Organization of the Studies

(*a*) *Györ-Sopron County.*—The county's public health and epidemiological station was requested to collect faecal samples from a total of 160 children, selecting 20 children from each of the three towns and five districts of the county. The children were to fall equally in the five age-groups as follows: 3 to 23 months, 2 and 3 years, 4 and 5 years, 6 to 9 years, and 10 to 15 years, and only one child was to be chosen from the same child community (nursery, kindergarten). The schedule of sampling was as follows. Three samples were to be taken from every selected child in the period from one to five days before each feeding ; post-vaccination samples were to be taken at 3, 5, 12, 15, 22, and 24