Anticoagulants in Congestive Heart Failure

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Kinsey and White (1940) found clinical evidence of pulmonary infarction in 14% of patients surviving episodes of cardiac failure and in 29% of those dying in heart failure but not submitted to necropsy. Where necropsy was carried out the incidence of pulmonary infarction was found to be nearly 50%. Wishart and Chapman (1948) found clinical or necropsy evidence of pulmonary embolism in only 6.5% of patients with congestive heart failure given bishydroxycoumarin (dicoumarol) prophylactically. Subsequent trials have shown an incidence of thromboembolic complications ranging from 2% to 7% in congestive-failure patients given anticoagulants, as compared with 8% to 33% of controls (Anderson and Hull, 1950 ; Harvey and Finch, 1950 ; Griffith, 1952 ; Thorsen, 1957). As a result of such evidence, routine administration of anticoagulants to patients in congestive heart failure has been recommended (*Brit. med. J.*, 1963 ; Owren, 1963).

The apparent benefits of prophylactic anticoagulant therapy have to be weighed against its difficulties and dangers. Recent advances in the general treatment of congestive failure may, by shortening the period of bed-rest required, have reduced the risk of thromboembolic complications in this condition. The following controlled trial was undertaken to reassess the risk of these complications and to define the place of anticoagulants in a modern congestive-failure regimen.

Methods

Patients with congestive cardiac failure, admitted under the care of one consultant physician to one ward of the hospital during the period April 1962 to April 1965, formed the basis of the study. Alternate patients were given prophylactic anticoagulant therapy unless there was a specific contraindication such as peptic ulcer. Patients with a contraindication were not excluded from the trial but were placed in the "control" group. Apart from the anticoagulant drug, therapy was generally similar in both "treatment" and "control" groups.

The anticoagulant used was phenindione, and therapy was begun with a single dose of 100 mg. on the first day followed by two doses of 50 mg. on the second day. Dosage thereafter was adjusted to prothrombin time (Quick's method), the aim of treatment being to maintain the patient's prothrombin time at two to two and a half times control. This level of prothrombin was attained by the end of the first week in most cases. Higher initial doses were avoided because of the congestive hepatomegaly. Heparin was not used in this series.

Details specifically noted on admission included age, sex, degree and cause of congestive cardiac failure, presence of atrial fibrillation, and history of previous thromboembolic episodes. The degree of congestive failure was judged to be mild, moderate, or severe on clinical grounds, chiefly on the amount of dependent oedema.

The occurrence of venous thrombosis or pulmonary embolism during the trial was carefully noted, the diagnosis being made clinically or at post-mortem examination, which was performed in 21 of the 31 fatal cases (11 necropsies in the anticoagulated group and 10 in the control group).

Material

The records of three of the 159 patients who entered the trial were inadequately completed. Of the remaining 156, 76 received anticoagulant therapy and 80 did not. Table I summarizes the findings in each group with regard to sex, age, degree of heart failure on admission, presence of atrial fibrillation, cause of cardiac failure, history of previous thromboembolic episodes, and duration of bed-rest during treatment in hospital. It will be seen that there was no significant difference between the two groups with respect to any of these criteria. There was no reason to suspect any difference between the groups with regard to period of bed-rest at home before admission to hospital but we have no accurate information on this point.

TABLE I.—*Comparison Between Anticoagulated and Control Groups with Regard to Age, Sex, Degree, and Cause of Heart Failure, Presence of Atrial Fibrillation, Previous Thromboembolic Episodes, and Duration of Bed-rest While in Hospital*

	Anti-coagulated Group	Non-anti coagulated Group	P
Mean age	59·2	57·4	> 0·8
Sex: Male	31	36	> 0·5
Sex: Female	45	44	
Degree of heart failure: Mild	17	16	> 0·8
Degree of heart failure: Moderate	29	28	
Degree of heart failure: Severe	30	36	
Atrial fibrillation: Present	44	36	> 0·1
Atrial fibrillation: Absent	32	44	
Cause of heart failure*: Rheumatic	45	39	> 0·5
Cause of heart failure*: Hypertensive	12	15	
Cause of heart failure*: Coronary	18	17	
Cause of heart failure*: Pulmonary	6	9	
Cause of heart failure*: Others	5	8	
Previous (venous) thromboembolic episode	8	4	> 0·3
Duration of bed-rest: 0–7 days	9	9	> 0·3
Duration of bed-rest: 8–14 „	10	17	
Duration of bed-rest: 15–28 „	43	35	
Duration of bed-rest: 29+ „	14	19	

* Two aetiological factors were present in 10 cases in the anticoagulated group and in eight cases in the control group. This accounts for the apparently high totals in this section.

Results

Overall Mortality.—There were 13 (17%) deaths in the anticoagulated group and 18 (22.5%) in the control group. This difference is not significant (P>0.3). Four of the deaths in the treated group and three in the control group were due to pulmonary embolism. The other causes of death are shown in Table II.

TABLE II.—*Cause of Death in Anticoagulated and Control Groups*

Cause of Death	Treated Group	Control Group
Pulmonary embolism	4	3
Myocardial infarction	1	2
Cardiac failure	5	7
Haematemesis	1	—
Ventricular fibrillation	—	1
Ruptured aortic aneurysm	1	—
Carcinomatosis	—	1
Hypertensive renal disease with uraemia	—	1
Operative death (mitral valve replacement)	1	—
Fulminating colitis	—	1
Pneumonia	—	2

Incidence of thromboembolism during the trial.—No episode of venous thrombosis uncomplicated by pulmonary embolism was recognized in either group. Pulmonary embolism occurred in 6 (8%) patients in the treated group and in 8 (10%) in the control group. This difference is not significant (P>0.5). Eleven of the episodes (seven in the control group and four in

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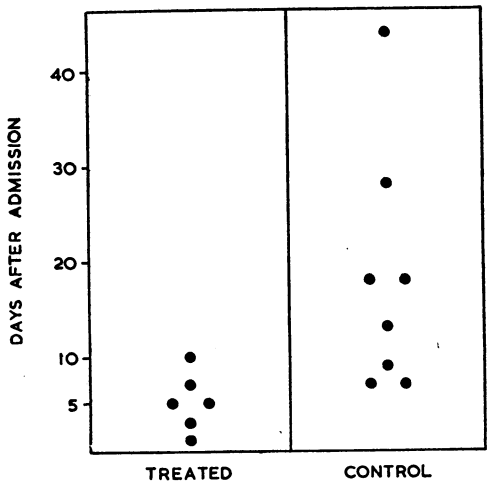
the anticoagulated group) were diagnosed on clinical grounds, confirmatory evidence being obtained in the three patients who came to necropsy. The remaining three cases of pulmonary embolism (one in the control group and two in the anticoagulated group) were first detected at post-mortem examination. The overall incidence of pulmonary embolism found at necropsy was 29%.

Time of occurrence of thromboembolism.—The time intervals between admission and occurrence of embolic episode (see Chart) were as follows:

Treated group: 1, 3, 5, 5, 7, 10 days Mean= 5.2 days
Control group: 7, 7, 9, 13, 18, 18, 28, 44 days Mean=18.0 days

The difference between the two groups is significant ($P<0.05$).



Time of occurrence of pulmonary embolism in patients receiving prophylactic anticoagulant therapy compared with a similar control group not receiving anticoagulants.

Influence of prior episode of thromboembolism on the risk of a further episode during the trial.—Of the eight patients in the treated group with a history of venous thromboembolism, one suffered pulmonary embolism during the trial. Four patients in the control group gave a history of a prior thromboembolic episode, and one of these had pulmonary embolism during the trial.

Other factors of possible relevance.—In view of the small number of incidents of thromboembolism during the trial it was not thought worth while to analyse the two groups separately in order to determine whether sex, age, degree and cause of heart failure, and presence of atrial fibrillation influenced the risk of thromboembolic episodes. This analysis was made, however, on the two groups combined, and the results are set out in Table III. It may be seen that age, sex, and presence of atrial fibrillation did not show any statistically significant effect on the occurrence of thromboembolism. However, it is noteworthy that no patient under the age of 50 suffered such an episode, although this group represented 20% of the patients in the trial. Patients with severe congestive cardiac failure were much more likely to suffer from thromboembolism than those with lesser degrees of failure. It was also noted that patients whose heart failure had been attributed to coronary disease appeared more prone to thromboembolism. It was initially thought that this might be due to a larger proportion of these coronary patients being in severe failure, but the records show that only 37% of this group were severely affected, compared with 44% of patients in other aetiological groups.

TABLE III.—*Influence of Age, Sex, Degree and Cause of Heart Failure, and Presence of Atrial Fibrillation on Risk of Thromboembolism*

		Thrombo-embolic Episode	No Thrombo-embolic Episode	P
Mean age		58·6	62·9	>0·1
Sex	Male	7	60	>0·5
	Female	7	82	
Degree of heart failure	Mild	1	32	<0·01
	Moderate	1	56	
	Severe	12	54	
Atrial fibrillation	Present	8	72	>0·5
	Absent	6	70	
Cause of heart failure	Coronary	5	30	<0·05
	Others	9	130	

Complications of Anticoagulant Therapy.—The only serious complication attributed to the therapy was terminal haematemesis in an 80-year-old man suffering from degenerative heart disease with severe congestive phenomena. Another patient died of a ruptured abdominal aortic aneurysm while taking phenindione in appropriate dosage.

Discussion

In this series pulmonary embolism was found in 29% of all patients in congestive cardiac failure coming to necropsy, in contrast with the 48% incidence reported by Kinsey and White (1940). The 10% incidence of thromboembolic complications found in our control group is comparable with the 8% incidence found by Anderson and Hull (1950) and the 15% incidence of Harvey and Finch (1950).

It appears that the chief factor influencing the risk of thromboembolism is the severity of congestive failure as judged clinically. Only two embolic episodes occurred in 90 patients with mild or moderate failure, but 12 such incidents occurred in 66 patients with severe failure. Age may play a part in so far as no episode occurred in a patient under 50 years old. There is a significant excess of incidents in the group with coronary heart disease. On this evidence it would appear that if effective prophylactic measures are available they should certainly be used in patients over 50 years of age and in severe congestive failure, and perhaps also in younger patients whose heart failure is due to coronary disease.

In this series no significant difference was found between the overall thromboembolic complication rates for the treatment and control groups. There was, however, a striking difference between the times of onset of embolic episodes in the two groups, all occurring within the first 10 days (mean, five days) in the treatment group and all after the first week (mean, 18 days) in the control group. This finding is not due to any obvious technical difference, such as varying necropsy rates in the two groups at the relevant time. It might well have been obscured if, as in some other trials, thromboembolic episodes occurring during the early days of anticoagulant therapy had been discounted on the grounds that the therapy was not by then "effective."

The implications of the difference in time of embolism here found must remain in some doubt, since we lack information regarding the period of domiciliary bed-rest, before admission to hospital, for the two groups. However, the two groups are so similar in all respects for which information is available that a significant difference in this regard seems unlikely. It is also the case that bed-rest at home is rarely as complete as is the rule in hospital, and that there was not one thromboembolic episode in the control group during the first six days after admission. The possibility that the early occurrence of thromboembolism in the anticoagulated group is in some way related to the anticoagulant therapy given must therefore be entertained.

There is some experimental evidence to suggest that small doses of heparin or dicoumarol may actually be thrombogenic (Merskey and Drapkin, 1965). If this is so, perhaps there is also an increased tendency to thrombosis during the early stages of oral anticoagulant therapy, before therapeutic prothrombin levels have been attained, and that some such mechanism may account for the early incidence of thromboembolism in the treatment group of this series.

It is concluded that anticoagulant drug prophylaxis is not mandatory in younger non-coronary-heart-disease patients with

mild congestive phenomena. In such cases it appears justifiable to rely upon physiotherapeutic measures while in bed, and early ambulation, to prevent venous thromboembolism. In the case of older patients with severe congestive failure, however, oral anticoagulant drug therapy can be expected to prevent venous thromboembolism after the second week, and such prophylaxis is clearly indicated if its possible early thrombogenic tendency can be overcome. Concurrent high-dosage intravenous heparin therapy during the first week or 10 days may surmount this difficulty, but, with the methods at present in use, would seriously interfere with the prothrombin estimations necessary for accurate adjustment of the dose of oral anticoagulant. Rapid attainment of therapeutically desirable prothrombin levels by means of heavier initial loading doses of a quicker acting oral anticoagulant such as ethyl biscoumacetate (Weiner *et al.*, 1955), perhaps with heparin for the first day or two, may offer a preferable alternative.

Summary

The incidence of pulmonary embolism in 76 patients with congestive cardiac failure given prophylactic (oral) anticoagulant therapy was 8%. The incidence in a similar control series of 80 such patients not given anticoagulants was 10%.

Anticoagulant prophylaxis with phenindione, instituted at the time of admission, appears to afford protection against venous thromboembolic complications after the first 10 days, but this advantage is counterbalanced by an apparently increased tendency to such episodes during the first week or 10 days of administration of the drug.

The risk of thromboembolism in patients with clinically mild degrees of failure is too small to warrant routine anticoagulant drug prophylaxis.

We gratefully acknowledge the keen interest taken by the late Dr. O. Brenner in the establishment of this trial and his kind permission to study patients under his care. Our thanks are due also to Dr. W. C. Smallwood for his helpful criticism and advice, and to Mrs. P. Moffat for her patient secretarial assistance.

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Pygopagus Conjoined Twins

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The occurrence of conjoined twins is rare. The incidence, according to Potter (1961) and Puegh (Guinard, 1893), is one in 50,000 births. Robertson (1953), in an analysis of 117 cases collected from the literature by Taruffi (1891–4), determined the sites of union. In 73% of the cases the junction was in the thoracic region (thoracopagus), in 19% it involved the sacral region (pygopagus), in 6% the pelvic outlet (ischiopagus), and in 2% the head (craniopagus). Though there are numerous detailed reports of the separation of craniopagus and thoracopagus conjoined twins, no account of the separation of pygopagus and ischiopagus conjoined twins is to be found in the medical literature.

Case Report

These female conjoined twins (Joan and Jennifer) were self-delivered at home on 24 December 1961 to a 25-year-old Nigerian woman who had five other children. The mother stated that the first twin was born by the head, followed by the four legs and then the head of the second baby. After delivery the mother's general condition was good and her perineum was intact. There was a history of twinning in the father's family. The combined weight of the twins at birth was 3,640 g. During their stay in Nigeria, Jennifer (the left-sided twin) had a severe chest infection, and frequent watery stools were passed from the common anus. The twins were vaccinated separately on 21 March 1962, but as the vaccination did not take in Jennifer she was revaccinated on 26 March, when it took satisfactorily. They were transferred to Hammersmith Hospital on 6 April under the care of Professor Ian Aird.

The twins were joined at the buttocks, there being complete fusion of the left buttock of one with the right buttock of the other and incomplete fusion of the other buttocks, so that they were not completely back to back but could turn their heads to look at each other. Joan was on Jennifer's right-hand side (Figs. 1 and 2). The anal opening was common to the twins, but it was situated more to Joan's side. The external genitalia were separate.

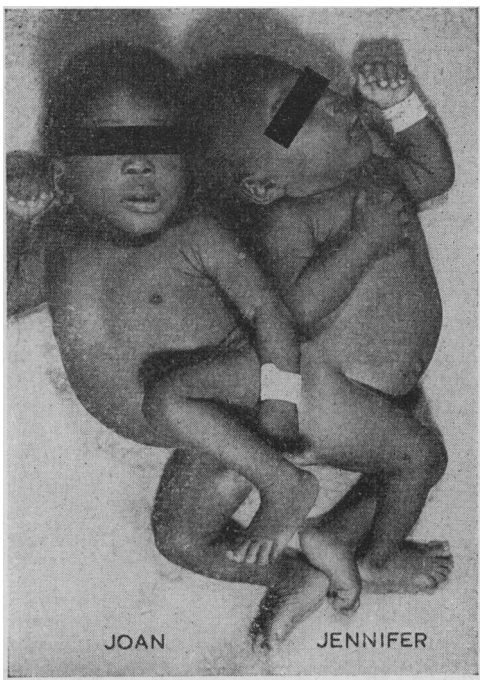

FIG. 1.—Twins before separation.

On admission to Hammersmith Hospital Joan was observed to be more lively and active that her sister. She had a grade 3/6 pansystolic murmur over the third and fourth left intercostal spaces parasternally. Lungs and abdomen showed no abnormality. Cervical, thoracic, and upper lumbar spine were normal except for

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