**Part II—Natural history**

**Summary**

Seven out of 76 patients who had sustained a cerebrovascular accident suffered a pulmonary embolism as diagnosed at necropsy or by unequivocal antemortem criteria. A further five patients had probable embolisation diagnosed only by clinical and chest x-ray criteria. Eleven of these 12 patients had DVT as diagnosed by the $^{125}$I-fibrinogen technique. Though $^{125}$I-fibrinogen technique has its limitations, thrombosis seemed to be able to develop at several independent sites in the venous system of the leg.

**Introduction**

In Part I we showed that the incidence of deep venous thrombosis (DVT), as detected by the $^{125}$I-fibrinogen technique, in patients who had suffered strokes was 53%. We then examined the incidence of pulmonary embolism in the same patients. Since conventional anticoagulation is probably hazardous after recent cerebral infarction not due to arterial embolism,1 we were able to study the natural history of venous thromboembolic disease.

**Patients and methods**

The 76 patients were described in Part I, as were the methods of diagnosing DVT. Follow-up periods ranged from two months to two years.

Pulmonary embolism was diagnosed either by the doctors caring for the patients or at necropsy by the pathologists working in the Aberdeen University department of pathology. Definite pulmonary embolism was diagnosed only if there was either embolism at necropsy or very strong antemortem evidence. Probable pulmonary embolism was diagnosed on the basis of clinical symptoms and signs and chest radiography.

**Results**

Nineteen patients died in the 10-day study period (mortality rate 25%), and by the end of follow-up 43 patients were known to be dead (mortality rate 57%). Nine necropsies were carried out.

**INCIDENCE OF PULMONARY EMBOLISM**

Macroscopic pulmonary emboli were found in five of the nine patients who came to necropsy, and in one of these patients (case 4).
emboilism was the cause of death on the 30th day after the stroke (table 1). Two patients were thought to have definite pulmonary embolism on the basis of clinical investigation alone. One (case 2) developed pleuritic chest pain, haemoptysis, and a characteristically abnormal lung scan on the 28th day after stroke, and the second (case 3) developed acute cor pulmonale with characteristic electrocardiographic changes on the seventh day after stroke and died 48 hours later. Five patients were considered to have probable embolism but were not extensively investigated as they were elderly and in poor general health (table 1). The incidence of definite pulmonary embolism was therefore 9%, and of probable embolism 7%.

**Table 1**—Incidence of thrombi, diagnosed with 51-I- fibrinogen, related to position in leg at which thrombosis occurred and started (see Part I for diagram of leg positions)

<table>
<thead>
<tr>
<th>Leg positions</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of times each site was site of onset</td>
<td>10</td>
<td>3</td>
<td>13</td>
<td>12</td>
<td>22</td>
<td>29</td>
<td>39</td>
<td>31</td>
</tr>
<tr>
<td>Total No of positive scans at each site</td>
<td>16</td>
<td>6</td>
<td>1</td>
<td>12</td>
<td>16</td>
<td>27</td>
<td>27</td>
<td>16</td>
</tr>
</tbody>
</table>

Natural History
Clinical signs of DVT usually appeared four to seven days after the stroke, although the 51-I-fibrinogen test first showed positive results in 21 patients within three days of the stroke. After the 10-day study no patient was known to have developed clinical evidence of DVT.

The distribution of 51-I-fibrinogen positivity in the 45 limbs with DVT is shown in table 11. The total number of limbs with a positive scan at each position and the number of times any position was the point where a positive scan was first apparent are shown. If several positions became positive on the same day they were all included as positions of initial positivity. DVT seemed both to be most common and to start most commonly in the calf veins. In two patients DVT developed first in the thigh alone and in another patient in the popliteal fossa alone. Seven other patients developed two quite distinct areas of 51-I-fibrinogen positivity separated by one or more positions over which radioactivity was similar to that in the contralateral limb without DVT.

Of the seven patients with definite pulmonary embolism only one (case 7) did not have DVT diagnosed with 51-I-fibrinogen (table 11). This might be explained by the subclinical onset of DVT after the 10-day study since the embolism was detected only at necropsy 20 days after the onset of the stroke. One patient (case 5) had a 15% rise in radioactivity over the popliteal fossa, rather than the accepted 20%, for the diagnosis of DVT, but died the next day before rescanning. This finding probably represented the onset of thrombosis although at necropsy the leg veins were not examined. The five patients with probable pulmonary embolism all had DVT diagnosed with 51-I-fibrinogen. In five of the 12 patients with pulmonary embolism DVT appeared to be confined to the calf veins. If the patients who may have embolised after the study period were excluded, however, there remained only one (case 10) in whom DVT was confined to the calf at the time of embolisation; the diagnosis of embolism in this patient was uncertain, however, since it was made only on the appearance of an aterectatic area on the chest x-ray film.

**Discussion**
We have shown that DVT is a common complication of strokes (see Part I), and we have now found that incidences of definite and probable pulmonary embolism after strokes are 9% and 7% respectively. These figures are likely to be an underestimate since few patients come to necropsy, but they are similar to those reported by others. Clearly, therefore, about half the patients admitted to hospital after an acute hemiplegia or hemiparesis are likely to develop DVT in their paralysed leg, and about half those who come to necropsy will have evidence of pulmonary embolism. Although many of these patients are elderly and often expected to die as a result of their primary disease several may die as from pulmonary embolism and the rehabilitation of many others will be delayed because of the morbidity associated with both DVT and non-fatal pulmonary embolism. The further understanding of the pathogenesis and prevention of this common complication of strokes is therefore clinically important.

Most comprehensive necropsy studies have emphasised that DVT is more common in the calf veins than in proximal sites in the venous system, and our results, allowing for the insensitivity of the 125-I-fibrinogen technique in the upper thigh, support this view and are similar to those found with the same method in both surgical and medical patients. Nevertheless, the 125-I-fibrinogen studies usually continued for only about 10 days and the distribution of venous thrombi may have been different if patients had been studied longer.

It has been assumed, partly on the basis of results obtained with the 125-I-fibrinogen technique, that venous thrombosis usually starts in the calf and propagates proximally. This view may, however, be the result of a policy of early anticoagulation and the inaccuracy of the 125-I-fibrinogen technique in the upper thigh since most complete necropsy studies have shown that venous thrombosis usually occur in one or more independent sites. Our results support the necropsy findings since venous thrombosis, although often appearing first in the calf, also first appeared in the thigh or popliteal veins, and in seven of the 40 patients with thrombi in the paralysed leg more than one independent point of origin was found. The finding of independent origins of DVT has been reported by others using the 125-I-fibrinogen technique. It is difficult to interpret the spread of radioactivity due to the deposition of 125-I-fibrinogen. Indeed, apparent propagation of thrombi occurred both proximally and distally, but the technique cannot detect either thrombi in adjacent veins or the separation of thrombi by short segments of unoccluded veins. Indeed, the appearance of thrombosis spreading proximally up the leg veins over 24 hours between scans could be explained by the distal propagation of thrombus from an independent more proximal site that may not necessarily be detectable with 125-I-fibrinogen. Considering both necropsy and 125-I-fibrinogen evidence, however, venous thrombosis probably propagate either proximally or distally from several independent sites of origin in the venous system of the leg.

Undoubtedly most pulmonary emboli arise from venous thrombi in the legs or pelvis. The evidence, although circumstantial, is based on the fact that almost all adult patients with pulmonary embolism have venous thrombi in their legs, which are detected either at necropsy or during life. We our results support this view, since of the 12 patients with pulmonary embolism only one did not have a DVT diagnosed with 125-I-fibrinogen. In common with others we found that most patients with pulmonary embolism that occurred during the scanning period had DVT proximal to the calf. We can draw no conclusion about the site in the venous system from which these emboli originated, however. The necropsy evidence suggests that large embolii arise from the pelvic or thigh veins and the fact that the 125-I-fibrinogen test so often gives positive results, provided the fibrinogen is given before the onset or propagation of venous thrombi, in patients with pulmonary embolism is presumably because thrombi in the large proximal veins are usually associated with more distal small-vein thrombi. We cannot, however, reject the hypothesis that some pulmonary emboli, particularly small ones, may arise from venous thrombi in the lower part of the thigh or calf.

We thank the doctors of the Aberdeen teaching hospitals for permission to study patients under their care and Professor A L Stalker in whose department the necropsy examinations were undertaken.

**References**
Psychiatric morbidity and the menopause: clinical features

C BARBARA BALLINGER

British Medical Journal, 1976, 1, 1183-1185

Summary

A sample of 114 women from the general population aged 40-55 years were identified as possible psychiatric cases and subjected to a standardised psychiatric interview. Mean ratings for reported symptoms and observed abnormalities were assessed in relation to menopausal status. There was no evidence of any specific combination of symptoms and signs associated with the cessation of menstrual periods, though after the menopause insomnia and hypochondriacal preoccupations were more common. In comparison with matched normal controls there was more likely to have been previous psychiatric illness, and contact with general practitioners was more frequent. Many women developing psychiatric symptoms at the time of the menopause appear to belong to a vulnerable population who are likely to develop symptoms in relation to stress.

Introduction

Opinions on psychiatric illness occurring at the time of the menopause differ widely. Malleson stated that emotional symptoms at this time were precipitated by oestrogen deficiency and should be treated with oestrogen preparations. She described the symptoms as having a specific menopausal quality, different from those of psychiatric or psychogenic illness.

There has also been discussion about the nature of affective illness at this time of life. Kraepelin described a syndrome of "involutional melancholia," which he separated out from affective illness in general on the basis of age of onset and clinical features. The concept of involutional melancholia was not restricted to illness at the time of the menopause but applied to affective illness in both men and women in later life. Tait et al., in a study of women admitted to mental hospital for the first time between the ages of 40 and 55, were unable to find any evidence of a clinically distinct involutional type of illness or any relationship between the onset of the illness and the menopause. Nikula-Baumann, who studied affective illness in later life, concluded that an involutional type of affective illness could be separated out on clinical grounds, but the mean age of onset of the illness was 56 years and usually it began several years after the menopause. The women in her study were said to have normal urinary gonadotrophin excretion but urinary oestrogen excretion less than in controls, although not significantly so.

In view of the variation in opinion about the clinical features of psychiatric illness at the time of the menopause, and in particular the claim that emotional symptoms and signs differ in some way from those occurring before the menopause, I decided to obtain detailed information on symptoms and signs in a group of women aged 40-55 years identified as possible psychiatric cases and to relate the findings to their menopausal status.

Method

As previously described, 760 women from the general population aged 40-55 years were screened for psychiatric illness using the general health questionnaire. Women who scored 12 or more on the questionnaire were regarded as possible psychiatric cases and invited to attend for interview. A standardised psychiatric interview schedule was used that was developed for use in community surveys and has been used in general practice. Individual symptoms are rated on a five-point scale, 0 indicating absence of a symptom and 1 a habitual trait or borderline symptom. A rating of 2 or more indicates a definite morbid symptom of mild (rated 2), moderate (rated 3), or severe degree (rated 4). Manifest abnormalities observed during the interview are rated on a five-point scale immediately after the interview. An overall severity rating may also be made, 0 indicating no psychiatric illness and 1 mild or subclinical psychiatric illness. An overall rating of 2 or more indicates psychiatric illness of mild (rated 2), moderate (rated 3), or severe degree (rated 4).

A brief personal history was taken at the time of the interview, including information on relation with husband and any change in libido. Frequency of visits to the general practitioner, previous psychiatric illness, and prescribed medication were also noted for each woman. The same information was obtained for a group of women matched in respect of social class, menopausal status, and age who had obtained low scores on the general health questionnaire. These "non-cases" were used as normal controls.

Results

Out of 539 women who returned completed questionnaires 155 scored 12 or more; 11 of these had had a hysterectomy. Of the remaining 144 women, 114 (79%) agreed to the interview and were classified according to four subgroups—premenopausal (53 women), menopausal (26 women), less than six years postmenopausal (21 women), and six or more years postmenopausal (14 women).