## Anticoagulation in patients with atrial fibrillation

### Not safe and not cheap

EDITOR,—I am concerned about the potential widespread use of warfarin in asymptomatic atrial fibrillation encouraged by recent articles. Philip M W Bath and colleagues assert that overwhelming evidence from trials suggests that this treatment profoundly reduces strokes, carries small risks of bleeding, and is cost effective. I am sceptical; these trials have to be scrutinised closely and compared with real life.

Patients enrolled in these trials were carefully screened for the slightest characteristics that might place them at any risk of bleeding and were more likely to be more compliant than average. The Veterans Affairs stroke prevention in non-rheumatic atrial fibrillation study excluded 7444 out of 7982 eligible patients; 6·7% were entered.[2] The stroke prevention in atrial fibrillation study initially excluded 17 046 eligible patients.[3] Of the 1330 entered, 703 were considered to be ineligible; only 3·4% were entered. Although atrial fibrillation is more common with advancing age,[4] four of the five trials were in younger patients at lower risk. Only one trial was in older patients[5]; in this study the numbers of events (thromboses and bleeding) were identical in all groups. Despite careful patient selection there were more side effects and non-compliance with warfarin. Though warfarin has led to fatal bleeding, it may not reduce the incidence of major strokes as shown below.

I have analysed the data in three trials that have detailed the severity of strokes.[2 3 5] The results are striking (table). No doubt warfarin reduced the incidence of transient ischaemic attacks and minor non-disabling strokes, but none of the trials showed that the incidence of fatal and disabling strokes was reduced beyond statistical doubt. This reduction in mild strokes has been achieved neither safely nor cheaply. A Canadian study showed an annual rate of fatal or major bleeding of 2% despite excluding 94% of eligible patients.[6] A complication rate exceeding 1·3% is estimated to increase costs.[7] The incidence and severity of bleeding in ordinary clinical practice is probably even higher. The ratio of risk to benefit will probably also increase with time beyond the trials' short 1·3-2·2 years of follow up. Strokes tend to cluster in the first months after the diagnosis of atrial fibrillation[4] and survivors with atrial fibrillation tend to have a similar risk of recurrence to those in sinus rhythm.[9]

Clinicians may argue that several strokes in groups given warfarin occurred either when warfarin was stopped or with subtherapeutic anticoagulation. Warfarin withdrawal may induce transient rebound hypercoagulability that could enhance thrombosis. Patients in trials were seen every three to four weeks, each time by a doctor, and had their tablets counted to check for compliance. If anticoagulation was unsuccessful despite this stringent follow up clinicians are unlikely to be successful in their overstretched clinics.

SAAD M B RASSAM

Queen Mary's Hospital,
Sidcup,
Kent DA14 6LT

1 Bath PMW, Prasad A, Brown MM, MacGregor GA. Survey of use of anticoagulation in patients with atrial fibrillation. *BMJ* 1993;307:1045. (23 October.)
2 Ezekowitz MD, Bridgers SL, James KE, Carliner NH, Coling CL, Gornick CC, *et al.* Warfarin in the prevention of stroke associated with nonrheumatic atrial fibrillation. *N Engl J Med* 1992;327:1406-12.
3 Stroke Prevention in Atrial Fibrillation Investigators. Stroke prevention in atrial fibrillation study. *Circulation* 1991;84: 527-39.
4 Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham study. *Stroke* 1991;22:983-8.
5 Petersen P, Boysen G, Godteredsen J, Andersen ED, Andersen B. Placebo-controlled, randomised trial of warfarin and aspirin for prevention of thromboembolic complications in chronic atrial fibrillation. The Copenhagen AFASAK study. *Lancet* 1989;i: 175-8.
6 Connolly SJ, Laupacis A, Gent M, Roberts R, Cairns JA, Joyner C. Canadian atrial fibrillation anticoagulation (CAFA) study. *J Am Coll Cardiol* 1991;18:349-55.
7 Gustafsson C, Asplund K, Britton M, Norrving B, Olsson B, Marke L-A. Cost effectiveness of primary stroke prevention in atrial fibrillation: Swedish national perspective. *BMJ* 1992;305: 1457-60.
8 Sandercock P, Bamford J, Dennis M, Burn J, Slattery J, Jones L, *et al.* Atrial fibrillation and stroke: prevalence in different types of stroke and influence on early and long term prognosis (Oxfordshire community stroke project). *BMJ* 1992;305: 1460-5.
9 Boston Area Anticoagulation Trial for Atrial Fibrillation Investigators. The effect of low dose warfarin on the risk of stroke in patients with nonrheumatic atrial fibrillation. *N Engl J Med* 1990;323:1505-11.

*Severity of cerebrovascular accidents in patients given placebo, aspirin, or warfarin in three trials*[2 3 5]

| | Placebo | Aspirin | Warfarin | p Value (warfarin *v* placebo) |
|---|---|---|---|---|
| *Veterans Affairs stroke prevention in non-rheumatic atrial fibrillation* | | | | |
| No of cerebrovascular accidents (No of patients in arm) | 19 (265) | | 4 (260) | 0·001 |
| Severity: | | | | |
| No impairment | 9 | | | |
| Minor | 7 | | 3 | |
| Major | 2 | | 0 | 0·32 |
| Fatal | 1 | | 1 | |
| *Atrial fibrillation aspirin anticoagulation study* | | | | |
| No of cerebrovascular accidents (No of patients in arm) | 19 (336) | 17 (336) | 5 (335) | |
| Severity: | | | | |
| Transient ischaemic attacks | 3 | 2 | | |
| Minor | 2 | 1 | | |
| Non-disabling | 3 | 7 | | |
| Disabling | 7 | 4 | 4 | 0·13 |
| Fatal | 4 | 3 | 1 | |
| *Stroke prevention in atrial fibrillation* | | | | |
| No of cerebrovascular accidents (No of patients in arm) | 17 (211) | | 6 (210) | 0·01 |
| Severity: | | | | |
| Minimal | 10 | | 4 | |
| Moderate | 7 | | 2 | 0·093 |
| Fatal | 0 | | 0 | |

**Advice to authors**

Priority will be given to letters that are less than 400 words long and are typed with double spacing. All authors should sign the letter. Please enclose a stamped addressed envelope for acknowledgment.

### Underuse of warfarin is multifactorial

EDITOR,—Philip M W Bath and colleagues recently surveyed the use of warfarin in hospital inpatients with atrial fibrillation and found that many patients with chronic atrial fibrillation and no contraindications to anticoagulants were not prescribed warfarin.[1] We surveyed the use of warfarin by 50 randomly selected general practitioners working in this health district by means of a questionnaire presenting the different clinical features associated with atrial fibrillation in a 60 year old man with no contraindications to anticoagulation.[2] The table shows the results for the 42 general practitioners who replied.

*Use of warfarin in chronic atrial fibrillation by 42 general practitioners*

| | Always | Occasionally | Never | No answer |
|---|---|---|---|---|
| Chronic atrial fibrillation: | | | | |
| Alone | 1 | 4 | 37 | 0 |
| With mitral valve disease | 9 | 8 | 24 | 1 |
| With transient ischaemic attack | 1 | 12 | 28 | 1 |
| With cerebral infarction | 2 | 10 | 28 | 2 |

After the survey we developed guidelines for the use of warfarin in atrial fibrillation and distributed them to physicians and general practitioners locally. Three months later we did not see any change in the rate of new referrals to this hospital's department of haematology for monitoring international normalised ratios.

Despite strong evidence, patients with atrial fibrillation and no contraindications to warfarin are not receiving anticoagulation. The reasons for this are unclear. Perhaps the message is not being put across sufficiently well; further progress might be possible if national organisations —for example, the British Cardiac Society, Stroke Association, or British Geriatric Society—championed this issue. Understandably, doctors may also be concerned that the complication rate for warfarin used in atrial fibrillation in the different trials does not reflect what is seen in clinical practice because all the trials excluded a high proportion of potential participants with atrial fibrillation and because those who participated were monitored closely.

Finally, Bath and colleagues state that warfarin is contraindicated in people over 80. In our guidelines we have not included age as a contraindication because the main determinant of complications from warfarin is the presence of underlying problems such as peptic ulcer disease, uncontrolled hypertension, or repeated falls. Increasing age is associated with greater sensitivity to warfarin, but this effect can be overcome as the dose is tailored to the international normalised ratio. The risk of an embolic event during atrial fibrillation increases with age; if people over 80 do not have any contraindications to warfarin they should be

offered the benefits of this treatment as younger subjects are.

LINDSEY DOW
BERNADETTE BERTAGNE

Department of Care of the Elderly,
University of Bristol,
Blackberry Hill Hospital,
Bristol BS16 2EW

1 Bath PMW, Prasad A, Brown MM, MacGregor GA. Survey of use of anticoagulation in patients with atrial fibrillation. *BMJ* 1993;**307**:1045. (23 October.)
2 Kutner M, Nixon G, Silverstone F. Physicians' attitudes towards oral anticoagulants and antiplatelet agents for stroke prevention in elderly patients with atrial fibrillation. *Arch Intern Med* 1991;**151**:1950-3.

## GPs not prepared for monitoring anticoagulation

EDITOR,—Philip M W Bath and colleagues suggest that, with the expected increase in patients taking warfarin for non-rheumatic atrial fibrillation, the management of long term anticoagulant treatment could be devolved into the community.[1] The haematology audit committee in North West Thames region is auditing the management of such treatment. As part of this audit we surveyed the general practitioners of 10 consecutive patients referred to each of 13 anticoagulant clinics throughout the region. We excluded three doctors from the same practices as others already recruited, and so a postal questionnaire was sent to general practitioners from 127 practices; 99 (78%) responded.

The 99 practices had a total of 1431 patients receiving anticoagulant treatment on their lists, with a median of 21 (range 1-50) patients per practice. The general practitioners reported that they were responsible for regulating the dose of warfarin for only 121 of the patients, and only 149 of the patients had blood specimens taken in the surgery. Eighty four of the general practitioners were satisfied with the service received from the hospital anticoagulant clinic. When asked about taking more control of their patients receiving anticoagulant treatment, 93 of the general practitioners did not want to run their own anticoagulant clinic—reasons given included insufficient time, knowledge, and training; lack of facilities; and a need for more finance. Although only three of the general practitioners had written guidelines on anticoagulation, 63 said that they would find such guidelines useful.

Our findings show that few patients receiving anticoagulant treatment in our region are managed by their general practitioner and few general practitioners are keen to take on this extra task. Before the management of anticoagulant treatment is devolved to primary care a substantial programme of education and guidance for general practitioners is probably required. In addition, the initiation and early management of warfarin treatment, during the period when patients are most at risk from bleeding,[2] may need to remain the responsibility of hospitals. We agree with Bath and colleagues that more resources are required to prevent strokes in patients with non-rheumatic atrial fibrillation. Prevention of the embolic complications of atrial fibrillation should release such resources,[3] and flexible approaches to the management of anticoagulation in primary and secondary care need to be evaluated.

FIONA TAYLOR
MARY RAMSAY

Haematology Audit Committee,
Academic Department of Public Health,
St Mary's Hospital Medical School,
London NW10 7NS

JENNIFER VOKE

Department of Haematology,
East Herts NHS Trust,
Queen Elizabeth II Hospital,
Welwyn Garden City AL7 4HQ

HANNAH COHEN

Department of Haematology,
St Mary's Hospital Medical School,
London NW10 7NS

1 Bath P, Prasad A, Brown M, MacGregor A. Survey of use of anticoagulation in patients with atrial fibrillation. *BMJ* 1993;**307**:1045. (23 October.)
2 Levine MN, Hirsh J, Landefeld S, Raskob G. Haemorrhagic complications of anticoagulant treatment. *Chest* 1992;**102**: 352-61S.
3 Gustaffson C, Asplund K, Britton M, Norving B, Olsson B, Marke L. Cost effectiveness of primary stroke prevention in atrial fibrillation: Swedish national perspective. *BMJ* 1992; **305**:1457-60.

## No consensus among doctors

EDITOR,—Philip M W Bath and colleagues state that "many patients with atrial fibrillation are not prescribed warfarin despite the absence of contraindications."[1]

Their finding from a retrospective study that there continues to be a low rate of introducing anticoagulation is not new. Our recent prospective survey of patients admitted as emergencies with atrial fibrillation to a district general hospital also showed a surprisingly low rate of introducing antithrombotic treatment.[2] Over six months only 20 of the 102 patients who had had atrial fibrillation were taking warfarin; 17 were taking aspirin.[2] Anticoagulation was given to only seven of the 150 patients who had not previously been given warfarin.[2] Consensus on treatment therefore continues to be lacking among physicians for the introduction of anticoagulant treatment, despite evidence from five randomised controlled trials.[2]

Despite the suggestion that warfarin should be used even in patients with paroxysmal atrial fibrillation[1] the risk-benefit profile for warfarin treatment has not been established in such patients (and the profile may be quite different from that in patients with chronic atrial fibrillation).[3] Therefore warfarin should be reserved for patients with paroxysmal atrial fibrillation who are at highest thromboembolic risk—including those with the sick sinus syndrome, frequent paroxysms of the arrhythmia, a previous thromboembolic event, or structural heart disease.[3] Aspirin, by contrast, has less potential for major adverse reactions and should provide sufficient prophylaxis for most other patients with paroxysmal atrial fibrillation.[3] Many patients with paroxysmal atrial fibrillation also have concomitant underlying ischaemic heart disease, which may benefit from the use of aspirin.

Although aspirin has been advocated as prophylaxis against thromboembolic events, in some patients with chronic atrial fibrillation its use has not been fully substantiated by the recent large studies. Aspirin would be preferable to warfarin if it were equally effective, if only for its ease of administration. The results, however, remain inconsistent. For example, the Copenhagen atrial fibrillation aspirin anticoagulation study showed no benefit from aspirin 75 mg daily, but this study was in an older population.[4] The stroke prevention in atrial fibrillation study reported that aspirin 325 mg daily had some beneficial effect, but not in patients over 75; it also did not prevent severe strokes.[5] Sadly, the use of aspirin remains controversial.

GREGORY Y H LIP

Department of Medicine,
University of Birmingham,
Dudley Road Hospital,
Birmingham B18 7QH

1 Bath PMW, Prasad A, Brown MM, MacGregor GA. Survey of use of anticoagulation in patients with atrial fibrillation. *BMJ* 1993;**307**:1045. (23 October.)
2 Lip GYH, Tean KN, Dunn FC. Atrial fibrillation in a district general hospital. *Br Heart J* (in press).
3 Lip GYH, Metcalfe MJ, Rao AP. Management of paroxysmal atrial fibrillation. *Q J Med* 1993;**86**:467-72.
4 Petersen P, Boysen G, Godtfredsen J, Andersen ED, Andersen B. Placebo controlled, randomised trial of warfarin and aspirin for prevention of thromboembolic complications in chronic atrial fibrillation: the Copenhagen AFASAK study. *Lancet* 1989;i:175-9.
5 Stroke Prevention in Atrial Fibrillation Investigators. Stroke prevention in atrial fibrillation study, final results. *Circulation* 1991;**84**:527-39.

## Use of warfarin dependent on local services

EDITOR,—The observation of Philip M W Bath and colleagues that many patients with atrial fibrillation were not given long term warfarin or aspirin as prophylaxis against stroke is not surprising.[1] Previous studies have shown that despite the proved efficacy of warfarin in primary stroke prevention in atrial fibrillation, doctors remain reluctant to prescribe oral anticoagulant treatment for their elderly patients.[2]

The Veterans Affairs stroke prevention in non-rheumatic atrial fibrillation study was a randomised study of 228 patients aged over 70, 88 of them being over 75.[3] It confirmed that the benefits of warfarin applied to people over 70, with a 79% reduction in the risk of first stroke, and that the rate of bleeding complications was not increased in older people.

The use of anticoagulation in atrial fibrillation is dependent on local clinical services achieving complication rates comparable with those in the published trials. If warfarin is to be widely used in older patients, in whom there is clear and proved benefit, local anticoagulation services must be able to deliver care to them. If, as Bath and colleagues suggest, the unpublished results of the European atrial fibrillation trial show a beneficial effect for warfarin in secondary stroke prevention the matter is further complicated. Patients with atrial fibrillation and recurrent stroke are likely to be more frail; to have coexistent disease; to be receiving concomitant drug treatment, which increases the risk of interaction with anticoagulants; and to be less able to attend hospital outpatient clinics.

Physicians have understandable concerns about prescribing warfarin for elderly patients because of fears about haemorrhage or drug compliance. The usual contraindications to anticoagulant treatment apply to elderly patients, just as to younger people, and dose requirements for warfarin decrease with age.[4] Studies have shown, however, that when prothrombin time is monitored regularly haemorrhagic complications from warfarin treatment can be avoided in elderly people.[5]

If government firmly believes that it can achieve the targets stated in *The Health of the Nation* there should be a case for introducing anticoagulation in atrial fibrillation as a health promotion strategy in general practice.

JANICE E O'CONNELL
CHRISTOPHER S GRAY

Bensham Hospital,
Gateshead Hospitals NHS Trust,
Gateshead,
Tyne and Wear NE8 4YL

1 Bath PMW, Prasad A, Brown MM, MacGregor GA. Survey of use of anticoagulation in patients with atrial fibrillation. *BMJ* 1993;**307**:1045. (23 October.)
2 Kutner M, Nixon G, Silverstone F. Physicians' attitudes towards oral anticoagulants and antiplatelet agents for stroke prevention in elderly patients with atrial fibrillation. *Arch Intern Med* 1991;**151**:1950-3.
3 Ezekowitz MD, Bridgers SL, James KE, Carlinger NH, Colling CL, Gormick CC, *et al.* Warfarin in the prevention of stroke associated with nonrheumatic atrial fibrillation. *N Engl J Med* 1992;**327**:1406-12.
4 James AH, Britt RP, Raskino CL, Thompson SG. Factors affecting the maintenance dose of warfarin. *J Clin Pathol* 1992;45:704-6.
5 Wickramasinghe LSP, Basu SK, Bansal SK. Long term oral anticoagulant therapy in elderly patients. *Age Ageing* 1988;17: 388-96.

## Don't deny treatment to elderly people

EDITOR,—In the paper surveying the use of anticoagulation in patients with atrial fibrillation, Philip M W Bath and colleagues recommended that patients over the age of 80 should not be given anticoagulant drugs because the risks are high.[1] This statement is unsupported by evidence. The benefits of anticoagulation are now well accepted.[2,3] Since a stroke at any age is catastrophic, any therapy which reduces the incidence