Table 2. Factors associated with delay of more than four weeks' duration (for 53 patients) between presenting to their general practitioners with symptoms of malignancy and the GPs making a referral.

Delay factor	No. of occurrences
Gradual evolution of symptoms or signs	16
Symptoms treated as benign	15
Patient aged less than 50 years	13
Reassurance by negative results of investigations[a]	9
Patient delay after presentation	5
Presentation with metastases	5
History of similar benign symptoms	5
Other medical problem	5
Patient aged over 85 years	3
Slow diagnostic process[b]	2

[a]For example, negative test result at stage at which undertaken, or inappropriate test to identify disease. [b]For example, abnormal test result led to a series of tests.

More than four weeks from the patient's first attendance was chosen arbitrarily to signify delay. While acknowledging that delay for various types of cancer will have different prognostic significance, the intention of the study was to identify why general practitioners may not recognize a malignancy within a reasonable time.

Most of the causes observed were those found by other studies[2] although, apart from Gray,[3] most researchers have considered one class of tumour and the causes of its delay. Delays in this study did not occur when patients presented with standard symptoms and were not associated with failure to examine.[4-6] Here patients aged under 50 years were more likely to experience delay than older patients presenting with similar symptoms. Although some tumours in younger patients may be more difficult to identify,[7] in the cases in the present study the general practitioner did not appear to be expecting a malignant cause for the symptoms.

Numbers in an individual practice are unlikely to be large enough to produce statistically significant conclusions, and a multicentre study to look at delays in general practice cancer diagnosis may be worthwhile.

JOHN B WILLIAMSON

PO Box 87-174
Meadowbank
Auckland 5
New Zealand

References

1. MacAdam DB. A study in general practice of the symptoms and delay patterns in the diagnosis of gastrointestinal cancer. *J R Coll Gen Pract* 1979; **29:** 723-729.
2. Ginzler M, Pritchard P, Mant D. Delay in diagnosing and treating cancer. Part 2: reasons for, and avoidance of, delay. *Oncol Pract* 1993; **1:** 4-10.
3. Gray DJP. The role of the general practitioner in the early detection of malignant disease. *Trans Hunterian Soc* 1966; **25:** 135-179.
4. Holliday HW, Hardcastle JD. Delay in diagnosis and treatment of symptomatic colorectal cancer. *Lancet* 1979; **1:** 309-311.
5. MacArthur C, Smith A. Delay in the diagnosis of colorectal cancer. *J R Coll Gen Pract* 1983; **33:** 159-161.
6. Springall RG, Todd IP. General practitioner referral of patients with lower gastrointestinal symptoms. *J R Soc Med* 1988; **81:** 87-88.
7. Lannin DR, Harris RP, Swanson FH, *et al.* Difficulties in diagnosis of carcinoma of the breast in patients less than fifty years of age. *Surg Gynaecol Obstet* 1993; **177:** 457-462.

Pneumococcal sepsis in a splenectomized patient

Sir,

Asplenic individuals are known to be at a higher risk of developing serious and potentially fatal sepsis.[1] Prophylactic measures are generally recommended for the first few years post-splenectomy.[2] We report a case of severe pneumococcal sepsis occurring more than 10 years post-splenectomy.

A 21-year-old man was admitted to hospital as an emergency with a 48-hour history of headache, neck stiffness, double vision, vomiting and diarrhoea. Fourteen years previously he had had an emergency splenectomy following a road traffic accident. He was not on prophylactic antibiotics and had not received pneumococcal vaccine.

On examination he was confused and febrile. Neurological examination revealed marked photophobia, neck stiffness, nystagmus and diplopia. As pneumococcal sepsis was clinically suspected, intravenous benzylpenicillin 2.4 g was given immediately. A computerized tomography brain scan undertaken before lumbar puncture was normal. Cerebrospinal fluid analysis showed the white blood cell concentration to be 71 mm^3 (polymorphs 76%, lymphocytes 24%), glucose <0.5 mmol l^{-1} (plasma glucose was 7.5 mmol l^{-1}) and protein 1.6 g l^{-1}. Numerous gram-positive diplococci were seen on microscopy. Pneumococci were later grown from both cerebrospinal fluid and blood.

Intravenous cefotaxime (2 g eight-hourly) and oral dexamethasone (4 mg six-hourly) were started, the latter being stopped after four days. Over the next 24 hours the patient began to improve but developed neurosensory hearing loss. On the sixth day after admission he developed a right hemiparesis. A repeat brain scan was normal. Cefotaxime was continued for 14 days. A further head scan showed a non-enhancing, low-density area in the left basal ganglia suggestive of infarction. Cerebrospinal fluid examination was repeated and no organisms were seen or grown on culture. He gradually improved and was discharged to a rehabilitiation unit. His major deficits were complete deafness in the right ear, mild hearing loss in the left ear and right hemiparesis with severe paralysis of the right arm and right foot. Following a four-week stay in the unit and continued physiotherapy thereafter, the patient was able to walk unsupported and to perform tasks of daily living.

Pneumococci are the commonest cause of sepsis in splenectomized individuals, accounting for up to 90% of such episodes.[3] Patients can present with an acute, febrile illness and treatment with appropriate antibiotics must be instituted promptly to reduce mortality and morbidity. Patients are susceptible throughout their lives but susceptibility is much higher during the first 2–10 years after splenectomy,[4] in children[5] and in those who have had an elective splenectomy (especially for haematologic malignancies and thalassaemia) rather than emergency post-traumatic splenectomy.[6]

In view of our patient's experience, we suggest that lifelong prophylactic antibiotics should be given, rather than only for the first two years post-splenectomy. Phenoxymethylpenicillin (penicillin V) is the drug of choice. Amoxycillin, if tolerated, may be a good alternative, particularly in children as it protects against *Haemophilus influenzae* as well as *Streptococcus pneumoniae.* Erythromycin should be used for patients allergic to penicillin.

Polyvalent pneumococcal vaccine should be offered and preferably given at least two weeks before elective splenectomy. It should probably be repeated every five years.[7] Vaccination in children aged less than two years may produce a poor antibody response. Meningococcal (groups A and C) and *Haemophilus influenzae* type b vaccines are also recommended. Patients should be warned of their increased risk of developing complications from malaria when travelling abroad, and should be advised to be meticulous with their antimalarial prophylaxis.

The above measures will not, however, completely prevent overwhelming sepsis[8] and asplenic patients (and their medical practitioners) need to be aware of their increased susceptibility, the need for prompt antibiotic treatment for symptoms of infection and for urgent referral for expert medical assessment. Patients should be supplied with a medic-alert

bracelet or card informing medical attendants during emergencies of their susceptibility.

E L C ONG
I S A HASSAN
M H SNOW

Infectious Diseases Unit
Department of Medicine
Newcastle General Hospital
Westgate Road
Newcastle upon Tyne NE4 6BE

References

1. Morris DH, Bullock FD. The importance of the spleen in resistance to infection. *Ann Surg* 1919; **79:** 513-521.
2. Waghorn DJ. Prevention of post splenectomy sepsis [letter]. *Lancet* 1993; **341:** 248.
3. van Wyke DB. Overwhelming post-splenectomy infection (OPSI): the clinical syndrome. *Lymphology* 1983; **16:** 107-114.
4. Schwartz PA, Sterioff S, Mucha P, *et al.* Post-splenectomy sepsis and mortality in adults. *JAMA* 1982; **248:** 2279-2283.
5. Pedersen FK. Post-splenectomy infections in Danish children splenectomized 1969-1978. *Acta Paediatr Scand* 1983; **72:** 589-595.
6. Dickerman JD. Splenectomy and sepsis: a warning. *Paediatrics* 1979; **63:** 938-941.
7. Anonymous. When to use the new pneumococcal vaccine. *Drug Ther Bull* 1990; **28:** 31-32.
8. Evans DIK. Fatal post-splenectomy sepsis despite prophylaxis with penicillin and pneumococcal vaccine. *Lancet* 1984; **1:** 1124.

Warfarin in stroke prevention

Sir,

In their review of the use of warfarin in atrial fibrillation, Sweeney and colleagues have highlighted some of the practical difficulties in realizing the potential benefit of this treatment in general practice in the United Kingdom (March *Journal,* p. 153). We feel that they have understated the evidence of effectiveness from a recent meta-analysis[1] as well as overstated the risks by not always considering bleeding episodes in control populations. A number of apparent inaccuracies are listed at the end of this letter. In addition, there are three important clinical questions worth considering.

Is the reduction in incidence of strokes and death worthwhile? A useful way of considering this is by determining the number of patients that have to be treated with warfarin for one year to prevent one event (death, stroke, systemic embolus or transient ischaemic attack). We calculate from the meta-analysis that for patients aged over 64 years, this is between 14 and 56, depending on age and the existence of other risk factors, specifically hypertension, diabetes and previous cerebrovascular events (Table 3). This compares favourably with treatment of hypertension where 469 patient-treatment years were necessary to prevent one stroke in the 16 trials reported in the meta-analysis by Collins and colleagues in populations with a mean age of 52 years.[2]

Is aspirin just as good as warfarin? For stroke and emboli prevention aspirin is approximately half as effective as warfarin and has no proven effect on overall death rate.[1] Warfarin reduces deaths by a third. This makes aspirin a second choice for most patients aged over 64 years who have atrial fibrillation, although it is certainly better than no treatment.

Are there ways of reducing the problems of warfarin therapy? Warfarin therapy is difficult to manage in general practice. The benefits outweigh the risks when therapy is carefully monitored in clinical trials; the challenge is to attain a similar quality of management in general practice. With only 15 patients with atrial fibrillation on an average general practitioner's list, and only one or two new cases per year, this should not be impossible. One option is the employment of specialist liaison nurses. We would welcome hearing from any readers who have experience of this, or any other, innovative organizational solution.

We also noted a number of important inaccuracies in the paper; these are listed in the order of the article rather than their potential importance.

The authors state that '40 patients with atrial fibrillation would have to be given anticoagulant treatment for one year to prevent one stroke. For every 1000 patients treated for one year, between 15 and 50 episodes of ischaemic stroke or systemic embolism would be avoided, at a cost of between four to six major episodes of bleeding over the same period'. According to our calculations, 33 patients would have to be treated for one year to prevent one stroke. For every 1000 patients treated for one year, between 26 and 42 strokes or systemic emboli would be prevented at the cost of three episodes of major bleeding.

On Table 1, the column heading 'relative risk of warfarin (%)' should read 'risk reduction with warfarin (%)'. The Boston area anticoagulation trial for atrial fibrillation (BAATAF) study was not a comparison of warfarin and aspirin; the comparison was of warfarin and no treatment although the control group could take aspirin.

On Table 2, the data in the first and second columns relating to the percentage of study days where anticoagulant control fell above or below the stated range are transposed for both the Copenhagen study of warfarin and aspirin for the prevention of thromboembolic complications in atrial fibrillation (AFASAK) and the stroke prevention in atrial fibrillation study (SPAF). Also on Table 2, the data referring to minor bleeding are cumulative prevalence rates for the whole follow-up period which varied from 1.3 to 2.5 years. The column heading should state this clearly as the implication could be that it is an annual rate.

On Table 3, the final paper by Landefield is a systematic review of 19 886 patients (3931 patients from randomized controlled trials, 4318 from inception cohorts and 11 637 from non-inception cohorts). The annual rates of fatal, major, and major and minor combined bleeding were 0.6%, 3.0% and 9.6%, respectively. Such a systematic review is likely to provide a stronger basis for discussion and action than the 10 much smaller studies quoted by Sweeney and colleagues.

STEPHEN MORGAN

DAVID MANT

Primary Medical Care
Faculty of Medicine
University of Southampton
Aldermoor Health Centre
Southampton SO16 5ST

References

1. Atrial fibrillation investigators. Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation. *Arch Intern Med* 1994; **154:** 1449-1457.
2. Collins R, Peto R, MacMohan S, *et al.* Blood pressure, stroke and coronary heart disease. Part 2: short-term reductions in blood pressure: overview of randomized drug trials in their epidemiological context. *Lancet* 1990; **335:** 827-838.

Table 3. Estimated number of patients with atrial fibrillation who have to be treated with warfarin for one year to prevent one event (death, stroke, systemic embolus or transient ischaemic attack).

	No. of patients needing warfarin who have	
Age (years)	No additional risk factors[a]	1+ additional risk factors[a]
<65	Infinite	31
65–75	31	25
>75	56	14

[a]Additional risk factors are a history of hypertension, diabetes, stroke or transient ischaemic attack.