increase recruitment are imperative. One recent landmark American trial took four years to enrol 129 patients¹⁵; over the same period some 40 000 new cases of oesophageal cancer were diagnosed in the United States.

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Aspirin and pre-eclampsia

Aspirin should not be used routinely to prevent or treat pre-eclampsia

The possibility of using aspirin to prevent pre-eclampsia and its complications stemmed from the results of several small controlled trials. These suggested that aspirin reduced the incidence of proteinuric hypertension and major complications such as intrauterine growth retardation and fetal death.¹⁻³ The theoretical basis of these benefits is believed to be aspirin's suppression of thromboxane synthesis, which results in less placental aggregation⁴ and therefore less placental ischaemia (thought to underlie impaired fetal growth and the clinical features of pre-eclampsia).

But concern has been expressed about the potential toxicity of such a potent antiplatelet drug for mothers and fetuses, and questions have been raised about the wisdom of generalising from the results of small trials in highly selected patients. The recent collaborative low dose aspirin study in pregnancy (CLASP) was designed to establish the relative benefits and risks of taking low dose aspirin to prevent or treat pre-eclampsia and intrauterine growth retardation.⁵

In this multicentre trial 9354 pregnant women were randomised to either daily aspirin (60 mg) or placebo. To simulate real obstetric practice the entry criteria were broad and embraced women thought to be at risk of pre-eclampsia or intrauterine growth retardation who were from 12 to 32 weeks pregnant. Primiparous women; women with pre-existing hypertension or a history of intrauterine growth retardation, pre-eclampsia, or stillbirth; and women with established pre-eclampsia could all be entered in the study.

The results were disappointing for everyone hoping for clear cut answers. Aspirin did not significantly affect the primary end points: proteinuric eclampsia, intrauterine growth retardation, stillbirth, or neonatal death. Preterm delivery was slightly (but significantly) less likely in women taking aspirin. Although post hoc analyses must be regarded with caution, they showed a significant trend for greater reductions in the incidence of proteinuric pre-eclampsia the earlier the preterm delivery. Importantly, for those women

taking aspirin neither placental haemorrhage nor maternal bleeding during epidural anaesthesia was more likely; women taking aspirin, however, required more blood transfusions after delivery. This study therefore found that low dose aspirin was safe for the fetus and newborn infant but did not clearly improve fetal outcome or maternal morbidity.

This trial was by far the largest to use antiplatelet drugs to prevent or treat pre-eclampsia and it dominates the meta-analysis of 17 published trials also reported by the authors of this study.⁶ These trials included over 15 000 patients and were heterozygous in design and selection of patients. Doses of aspirin varied, and some studies included dipyridamole as an antiplatelet agent.⁶ Overall, aspirin reduced the relative risk of proteinuric pre-eclampsia by a quarter—in keeping with the non-significant trend in this direction that was found in the collaborative low dose aspirin study in pregnancy. But the small reduction in the risk of perinatal death was not significant.

The results of this meta-analysis should be regarded with caution because it did not include unpublished, negative studies. The second largest trial included in the meta-analysis (of more than 3000 patients) also found no benefit of aspirin in preventing pre-eclampsia or perinatal mortality,⁷ but, disquietingly, use of aspirin was associated with a significant increase in antepartum haemorrhage. This study may have included higher risk patients who might have been more likely to develop haemorrhagic problems than those in the collaborative low dose aspirin study in pregnancy.

Why then did the earlier small trials suggest such substantial benefits for aspirin? Were there critical differences in the selection of patients, and was randomisation always unbiased? The results of the collaborative low dose aspirin study in pregnancy may have been diluted by the broad selection criteria and the wide ranging patterns of care across the different countries in the study. Possibly, 60 mg of aspirin is at the lower end of a dose-response curve yielding benefit, even

though other studies have reported that this dose is effective.

What conclusions can be drawn at this stage? Firstly, any benefits of low dose aspirin for patients at risk of pre-eclampsia (at least as defined by current criteria) are uncertain. At best, it is likely to benefit only a minority. Secondly, subgroup analysis suggests that those with a history of early pre-eclampsia and preterm delivery may benefit more. Such patients are particularly likely to have had hypertension or renal disease. For these patients the risk of problems in subsequent pregnancies is particularly high; the collaborative study suggests that the risks of treatment are small.

The authors of the low dose aspirin study rightly conclude that the results of their own and previous studies do not justify routine prophylaxis or the therapeutic use of antiplatelet treatment in all pregnant women who are at risk of pre-eclampsia or intrauterine growth retardation. In fact, late entry to the collaborative study for therapeutic reasons was, if anything, associated with increased perinatal mortality. Obstetricians may consider treating women before 20 weeks of pregnancy who have a history of early pre-eclampsia, but

clearly this excludes most women for whom aspirin was hoped to provide benefit. We still have a long way to go before we have really effective means of preventing or controlling this complex condition.

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Syncope

An accurate history tells all

Any lay person can recognise a common faint. Doctors find the diagnosis more difficult and complicate matters further by describing the condition as vasovagal or vasodepressor syncope. To be fair, doctors see more of the people whose faints are atypical and therefore tend to feel uneasy when someone loses consciousness in a public place. Hospital doctors' disquiet is compounded nowadays by the lack of a reliable and reproducible diagnostic test. When people who faint present to hospital, therefore, they tend to be subjected to expensive investigation. Every decade or so there is a reminder that such tests are unnecessary.^{1,2}

Most people who faint do not consult a doctor. Hence the prevalence of fainting is difficult to gauge; nearly a quarter of an elderly population admitted to having fainted once in the previous 10 years.³ Patients with syncope (not quite the same thing as fainting) can account for 3% of all emergency visits to hospital, and one third of them may require admission.⁴

The diagnosis of a simple faint rests on the clinical history, including most of the following features: upright posture, an emotional or painful stimulus, gradual not sudden fading of consciousness, sweating, nausea, pallor, other manifestations of autonomic activity, and rapid recovery on lying down. Simple faints tend to occur, and recur, in young people.

On the basis of the history alone vasovagal syncope may be differentiated from situational syncope provoked by coughing, micturition, or postural change; sudden cardiac syncope due to arrhythmia or circulatory obstruction; metabolic disturbances such as hypoglycaemia; and fits. If doubt remains after a careful drug history and physical examination the best and most economic course of action for inexperienced doctors is to request an electrocardiogram and send the patient to a consultant physician. Vasovagal syncope will be the commonest diagnosis—occurring in 58% of those presenting with syncope to hospital in one series.⁵

Although these simple measures can identify the causes of most faints, difficulties may persist—for example, if the loss of consciousness is abrupt, if there are no provoking circumstances, or if the patient is middle aged with no history of

recurrent faints. Some further investigation is then required, although the results must be interpreted with caution.⁶ Ambulatory electrocardiography might seem sensible, but normal people exhibit a wide range of arrhythmias, mostly bradycardias in young people, and ectopy in elderly people; rarely does an arrhythmia correlate with symptoms. A cardiac event recorder is inappropriate because people who faint do not have time to activate the device. Exercise testing is helpful for those rare people whose faints are due to loss of vasomotor tone after effort but may be unsafe in people with effort syncope due to aortic stenosis or hypertrophic cardiomyopathy. Carotid sinus massage may produce alarming asystole, which may not be the cause of the syncope.⁷

Electrophysiological testing and programmed cardiac stimulation have little value unless there is clinical evidence of structural heart disease.⁵ Nothing can quite reproduce the circumstances of the faint, but head up tilt testing in which the victim is maintained at 60° for 45 minutes⁸ can be revealing.¹ The technique of testing, the additional challenge of isoprenaline, and the reproducibility of the test are all the subject of continuing discussion. But the tilt test may confirm the diagnosis of simple vasovagal syncope and has identified a group of patients for whom the term malignant vasovagal syncope has been coined. These are people with recurrent, severe, and otherwise unexplained syncope in whom a test gives a positive result; their clinical history is intermediate between those of vasovagal and cardiac syncope.

People who suffer simple faints do not die. Reports of people being scared to death must be treated with scepticism,⁹ at least in developed countries. But people who faint need reassurance, and a few may experience continuing morbidity¹⁰ owing to uncertainty about the next faint and its consequences. Dual chamber pacing can help some people with malignant vasovagal syncope, although predicting which ones is difficult.¹¹ Pacing might be thought to correct only the bradycardia and leave the hypotension untouched, but this is not necessarily so, and certainly the abruptness of the faint can be ameliorated.¹¹ Some people are helped by treatment with