Aspirin and the stomach

SIR,—Your leading article (10 January, p 91) conveys a most timely warning and your opening sentence, "The gastrointestinal side effects of acetylsalicylic acid affect a substantial minority of those taking the drug," merits printing in bold type.

The medical professorial unit at Oxford is carrying out an extensive five-year trial, initiated by Sir Richard Doll, of aspirin as a potential preventive of cardiovascular accidents in later life, using as subjects for the trial medical practitioners who are over 60 and have volunteered to participate. The trial is not yet complete but has been operating, I believe, for some three to four years. I was one of those who agreed to participate but had to withdraw when, after taking 500 mg of buffered aspirin daily for some 13 months, without any prodromal symptoms I sustained a massive gastric haemorrhage, confirmed by gastroscopy as arising from a relatively recent gastric ulcer. Never previously in a very busy professional life have I suffered from peptic symptoms, nor since the ulcer healed after two months' treatment with cimetidine (Tagamet) have I experienced peptic symptoms; and my haemoglobin level is appropriately maintained.

Although the Oxford trial is not yet complete it would be of interest, even at this stage, if the organisers of the trial could inform the profession of the number of participants who have had to withdraw on account of gastrointestinal bleeding or peptic symptoms.

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**We sent this letter to Sir Richard Doll, who with Mr Peto replies below.—ED, *BMJ*.

SIR,—We welcome the attention that Mr H H Langston draws to the possibility of aspirin having side effects. When we originally wrote to members of the British medical profession inviting them to collaborate in a randomised evaluation of the risks and benefits of aspirin we said, "One difficulty in conducting such a trial is that aspirin may have material side effects. Dyspepsia is already recognised; gastrointestinal haemorrhage probably occurs, but it is certainly rare; and some specialists suspect that aspirin may play a part in producing renal disease if used in conjunction with other analgesics. It would be necessary, therefore, to explain the balance of benefit and risk with peculiar care. Doctors, however, are in a particularly favourable position to assess the situation, and we wondered whether they might be willing to collaborate in a randomised trial on themselves. . . . The results of the study will be reviewed periodically and we shall, of course, inform you as soon as they enable us to reach any clear conclusion."

We also noted in our letter of invitation that what is often done in randomised trials is to keep the interim results completely secret unless unequivocal differences emerge before the scheduled end of the study. We remain of the opinion that the reasons for adopting such a policy are sound; and it would not, in our view, be proper to release premature information from this trial or from any other of the trials we are conducting.

For the moment, the best estimate of the benefits and side effects of daily aspirin that is available is that provided by the results of the six placebo-controlled randomised trials of daily aspirin following myocardial infarction, the two largest of which became available only in early 1980. These results were summarised, with references, in a *Lancet* editorial[1] a few weeks after we had drawn them to the attention of the British doctors who are taking daily aspirin, saying, "Gastrointestinal bleeding was diagnosed in about 1% per annum of aspirin takers, with haematemesis in 0·1% per annum"; we also pointed out, however, that there was "unequivocal evidence from the aggregate of these six trials that aspirin has prevented about one-fifth of the reinfarctions that would otherwise have occurred. Moreover, there have been somewhat fewer strokes among the aspirin-treated patients. Clearly, it is important to determine reliably whether comparable risk reductions can be anticipated by apparently healthy people." Now, a year later, we still have no more reliable information to add to this.

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RICHARD PETO

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[1] Anonymous. *Lancet* 1980;i:1172-3.

Adverse reactions to drugs

SIR,—I write with reference to the interesting article by Professor Michael D Rawlins (21 March, p 974) on the division of adverse drug reactions into "augmented" (type A) and "bizarre" (type B) groups. I would respectfully submit that his proposed classification fails to encompass an uncommon but clinically important group of such reactions—namely, those associated with drug withdrawal.

Withdrawal syndromes are well described after stopping several drugs—for example, β-adrenergic blockers[1] and clonidine.[2] In the case of beta-blockers there is evidence that the β-adrenergic receptors become hypersensitive during blockade, leading to increased responsiveness after stopping the drug.[3 4] It would appear that such reactions are related to the normal action of the drug (type A) but are also "qualitatively abnormal" and "bizarre" (type B).

May I therefore suggest that any proposed classification of adverse drug reactions should make specific reference to withdrawal syndromes.

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[1] Alderman EL, Coltart J, Wettach GE, Harrison DC. *Ann Intern Med* 1974;**81**:625-7.
[2] Pettinger WA. *N Engl J Med* 1975;**293**:1179-80.
[3] Boudoulas H, Lewis RP, Kates RE, Dalamangas G. *Ann Intern Med* 1977;**87**:433-6.
[4] Ross PJ, Lewis MJ, Henderson AH. *Lancet* 1979;ii:875-6.

Guide to ineffective and hazardous treatment

SIR,—While I appreciated Professor Michael Rawlins's comments about my book *Health Shock: A Guide to Ineffective and Hazardous Medical Treatment*, I would like to correct an impression given by his review (31 January, p 392). He says that the book concentrates unashamedly on risk. However, the main emphasis of the book, as can be gauged from the subtitle, is in fact on the use of *ineffective* or unnecessary treatment.

The author's introduction does state, for example, "The question of drug dangers and damage is surely not as important as the fundamental question of effectiveness . . . if a drug does not work in the first place it does not matter if it has harmful side effects because no one needs to take ineffective drugs in the first place." I also said that the book was not intended as a guide to medical treatment per se or as a guide to drugs, because there are plenty of books already available on these subjects.

The problem remains: where does a member of the public go when trying to find out if the drug he or she has been given is really necessary or effective? When doctors are guilty of indiscriminate use of untested or ineffective remedies on the scale demonstrated by Professor A C Cochrane in his book *Effectiveness and Efficiency*, Joe Citizen has reason to be wary of the advice from the average doctor. Similarly, how does a pregnant woman choose between a home and hospital birth when so much indiscriminate intervention in the birth process has now been shown to be harmful and unnecessary for most women receiving it?

Is it really necessary to restate the benefits of treatment? The medical profession will, I believe, be the first to tell you the benefits of what they are doing, but the last to tell you about the lack of need for what they are doing and the possible harm of what they are doing. Therefore the benefits of medical treatment, in my view, are well aired and well known. But the absence of benefit is something which has received scant attention until recently. Fortunately, it is the medical profession itself which is questioning medicine's effectiveness and by writing a book like *Health Shock* I tried to reflect this internal debate to a wider audience.

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Guidelines on the performance of chemical pathology assays outside the laboratory

SIR,—Pathologists are their own worst enemy. The guidelines (28 February, p 743) contain frequent reference to the *routine* laboratory. "Routine," according to the *Shorter Oxford* is a regular, unvarying, or mechanical procedure or discharge of duties. What an indictment of the profession.

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Status epilepticus treated by barbiturate anaesthesia

SIR,—I hesitate to cross swords with Drs E Sherwood Jones and A Luksza but I cannot allow their comments on barbiturate therapy to go unchallenged (28 February, p 741). There is now a considerable accumulation of published evidence not only for the efficacy of barbiturates in cerebral protection when given before an ischaemic-hypoxic insult, but also for a significant amelioration of neurological damage when given after the insult. Although