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We may return unduly long letters to the author for shortening so that we can offer readers as wide a selection as possible. We receive so many letters each week that we have to omit some of them. Letters must be signed personally by all their authors. We cannot acknowledge their receipt unless a stamped addressed envelope or an international reply coupon is enclosed.

Post-marketing surveillance of drugs

SIR,—I read the article by Dr A W H Marcus and his colleagues (21 July, p 163) with interest. These workers have shown that at the instance of the Committee on Safety of Medicines it is possible for a pharmaceutical company to identify a selected cohort of over 9000 hospitalised recipients of a new injectable drug and record brief details of its efficacy and toxicity for periods of several hours after the injection. Regrettably they did not give full details of the cost of the study, but from the information given it would seem unlikely to be less than £50 000. Thus, as a pilot study for a post-marketing surveillance programme of a new compound, this project seems to have been successful in its limited aims. It is important, however, to emphasise that it does not give much useful information on what is seen to be the main problem with new drugs—that of detecting reasonably common delayed adverse drug effects or effects arising only after long-term use of the new compound. For this purpose one requires to look to some of the proposed developments recently discussed in the *British Medical Journal* and elsewhere.¹⁻³ These studies all aim to identify a large cohort

of patients receiving a new drug and follow them for periods of up to one or two years. As yet none of the pilot studies currently under way have reported their results. Until they do it is important not to conclude, as Dr H Marcus does, that post-marketing surveillance studies are unlikely to add much to the knowledge and understanding of new drugs already gained from preregistration clinical trials.

Finally, I would take issue with Dr H Marcus and his colleagues when they state that “monitored release, however large the cohort size, without a suitable (randomised?) control group is a methodological impasse when rare effects are considered.” The objective of the proposed studies is to look for common (up to 1 in 500 recipients) serious events which may be drug related.⁴ If such events are noted in an uncontrolled screening programme such as carried out by Dr H Marcus then more detailed studies with different methods and incorporating appropriate controls are required to elucidate whether the event is truly drug related or not. The original screening studies can only be hypothesis-generating projects which, if successful, will require further

detailed studies before any outcome is accepted as being truly drug related.

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¹ Inman, W H W, in *Drug Monitoring*, ed M Gross and W H W Inman. New York, Academic Press, 1977.

² Dollery, C T, and Rawlins, M D, *British Medical Journal*, 1977, 1, 96.

³ Lawson, D H, and Henry, D A, *British Medical Journal*, 1977, 1, 691.

⁴ Lawson, D H, *British Journal of Clinical Pharmacology*, 1979, 7, 713.

Drug information and cost effectiveness

SIR,—The randomised controlled trial analysing the relative merits of buprenorphine and diamorphine by Dr M J Hayes and others (4 August, p 300) for the treatment of chest pain in suspected myocardial infarction is most interesting, but incomplete.

It is unfortunate that the authors of the study did not complement their careful analysis with an appraisal of the full economic costs of the different drugs. Buprenorphine is uncontrolled but more expensive to buy. The full costs of controlled and uncontrolled drugs can be estimated—see, for example, Culyer and Maynard’s analysis of the cost effectiveness of Fortral and morphine¹—and doctor decision makers should be given evidence not only of clinical efficacy but also of costs if we

are to ensure that their decisions are cost effective.

It is to be hoped that the appraisal work of Dr Hayes and his colleagues will be completed with a costing study in the near future.

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¹ Culyer, A J, and Maynard, A K, *Medical Care*, 1970, 8, 501.

Heatstroke in a "run for fun"

SIR,—The purpose of my letter (20 January, p 197) was to suggest that current medical literature may be inadequate on the subject of heat injury during "fun runs." The subsequent letter from South Africa is a good case in point (7 July, p 52). Professor T D Noakes and Dr L H Opie cite the monumental report of Malamud *et al*¹ to support their view that "sudden death due either to ventricular fibrillation or to cardiac arrest is not a feature of heatstroke." However, Malamud *et al* specifically excluded all instantaneous deaths from their study by limiting their cases to those collected from military hospitals and omitting 43 with inadequate clinical information. Instantaneous deaths and deaths soon after admission were not included. Thus, they do not touch on the question of sudden death due to heatstroke. Their pre-1946 report contained only a few electrocardiograms; but the necropsy finding of "fragmentation or rupture" of cardiac muscle fibres was present in "well over one-fourth of the cases"—a finding consistent with ventricular fibrillation.

I had hoped that we would not limit our concern to the "stroke" aspect of exertion-induced heat illness. The interplay of thermal damage, dehydration, and electrolyte disturbance can present as damage to one of several organs: kidneys, brain, heart, liver, or skeletal muscle. At necropsy, however, many tissues are damaged.

There have been three marathon-related deaths in the United States: the Boston *brain* death with six weeks' survival, a patient with *renal* failure who survived one week, and an instantaneous death due to *cardiac* arrest. The necropsies ruled out underlying organic disease in all cases. Although these three men could be described with Knochel's terms of "highly competitive, inexperienced, and over-enthusiastic,"² I believe that the sanctioning bodies should share some of the responsibility. At Boston they have, and this is now one of the safest marathons—with water every mile.

The scene in 1973 at Boston was quite different, however. Unregistered runners swelled the ranks to 1500. The race started at noon after an extremely unfavourable increase in heat and humidity. "International rules" stated that a runner could be "disqualified" if he accepted fluids from any source other than the "official tables." We gathered, sweating profusely, under a bright sun. The first water table was over 10 km away—holding only a fraction of the cups needed. About 500 runners, a third of the field, could not finish the 42 km. Fifty required medical care in hospital, five stayed overnight, and one died about six weeks later.

I regret that Noakes and Opie are not happy with my use of the term "heat stroke" in these cases. This disagreement is purely academic. I will accept any term they might

use for this syndrome of "multisystem damage during the marathon" so long as the preventive measures are the same as those for heatstroke.

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¹ Malamud, N, Haymaker, W, and Custer, R P, *Military Surgeon*, 1946, 99, 397.

² Knochel, J P, *Archives of Internal Medicine*, 1974, 133, 841.

The haematuria of the long-distance runner

SIR,—Your leading article (21 July 1979) does not contain any information about the frequency of haematuria after heavy exercise.

It may interest you to know that urine examinations just after the finish of the Norwegian marathon championship in summer 1978 showed that, of 41 participants being able to void a urine specimen within two hours, 13 showed a positive test (the method used was the Boehringer-Mannheim test-5L). Of the 13 positive tests, seven showed signs of erythrocytes, and six of haemoglobin. Control samples of the urine of these 13 runners one week after the competition showed completely negative test results. In addition to the 13 showing haematuria, three also had glucose in the urine after finishing, and these also had negative results in the control tests a week later.

I think that the phenomenon is more innocent than is suggested by your statement that "the doctor should assume that any haematuria . . . is due to underlying urinary tract disease until proved otherwise."

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Alcohol-dependent doctors

SIR,—Your leading article "Alcohol-dependent doctors" (11 August, p 351) refers favourably to the non-coercive New York state system to help the impaired doctor. The pilot scheme for anaesthetists based on these principles and initiated by the Association of Anaesthetists of Great Britain and Ireland and the Royal College of Psychiatrists (17 February, p 496) has only been operating for a short time. It seems already apparent that the scheme fills a gap in the present procedures and could usefully be extended to other branches of medicine.

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SIR,—Your leading article about alcohol- and drug-dependent doctors (11 August, p 351) is timely, because both patients and doctors need to be protected from the effects of one of the most insidiously growing threats to modern society. By admitting affected doctors to an institution it is comparatively easy today to stop them indulging themselves, but apart from this mere incarceration there is unfortunately little in the way of specific therapy that can be offered to them—which may well explain their readiness to discharge themselves against medical advice.

The results of current treatment in this

field are depressing, but nevertheless on historical grounds it can reasonably be expected that some spectacular breakthroughs in the management of diseases of the mind are long overdue. Until, however, such benefits accrue unquestionably the most important part of management is rehabilitation. In this context possibly the most vulnerable to poor management are young doctors who have not had time to put down roots—namely, junior hospital staff and assistants in general practice. In these cases the usual prelude to treatment is summary severance of whatever tenuous connections they may have formed within the community, with rehabilitation consisting of a rudderless drift from one unhappy locum post to another until some disaster renders successful and complete recovery a highly improbable eventuality. Like some of our learning-disordered children these hapless doctors are literally at the mercy of their environment.

Monitored treatment should therefore prove doubly helpful by ensuring that management as well as progress is properly supervised, because it should not be entirely forgotten that every doctor who is dependent on alcohol or drugs (or both) is somebody's very sick patient.

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Extracranial-intracranial anastomoses

SIR,—I was pleased to see the recent articles (7 July, p 2 and 18) and the letter (11 August, p 388) about extracranial-intracranial anastomoses: they reflect an increasing interest in this new and important neurosurgical procedure, and help, as Mr A K Keith Frazer says in his letter, to introduce the concept of cerebral revascularisation to a wider medical public.

May I make a plea to all those who ask for a biopsy of the superficial temporal artery and to those who frequently divide it not to do so until they have completely satisfied themselves that there is no alternative? The superficial temporal remains the most useful artery for cerebral revascularisation, and its absence can cause major technical problems.

Although it is 12 years since Professor Yasargil and Dr Donaghy performed the first anastomoses on patients, many questions remain to be answered about which patients are suitable for the procedure and what short-term and long-term benefits they can realistically expect from it. I believe that the answers can come only from neurosurgeons, neurologists, and neuroradiologists working closely together. To this end teams from Newcastle and Manchester have been participating for more than a year in the International Co-operative Study of Extracranial-Intracranial Arterial Anastomosis directed by Professor H J M Barnett of the University of Western Ontario. The results of this trial will be of interest to all concerned in the management of patients with cerebral ischaemia.

As Mr Keith Frazer also points out, extracranial-intracranial anastomoses are being increasingly frequently performed for conditions other than cerebral ischaemia. Clearly the full potential of this procedure, which, it must be acknowledged, is neurosurgical