hepatitis B virus is already fraught with difficulties. A good response (>100 mU antibodies to hepatitis B surface antigen/ml) is achieved in only 76.4% of adults and is less likely with increasing age; the vaccine is expensive, and uptake among health service workers is low.⁶ These problems must not be compounded by use of an inappropriate site of injection.

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- 1 Henley M. Site of injection for vaccination. *BMJ* 1992;305:184. (18 July.)
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Too deep or not deep enough?

EDITOR,—The 11 July issue of the *BMJ* makes intriguing reading, not least the correspondence column. Richard Park and Peter R Mills are upset that critics "did not read our study more carefully,"¹ while Ian Forgacs suggests that another critic "may have read our editorial rather too closely."² In the news section Linda Beecham announces the launch of the *Student BMJ*; one of its aims is to encourage the reading of scientific papers.³ Perhaps the *Student BMJ*'s recommendations for the required depth of study per article should be shared with the *BMJ*'s readers.

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- 1 Park RHR, Mills PR. Percutaneous endoscopic gastrostomy feeding. *BMJ* 1992;305:116. (11 July.)
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Outcome in the chronic fatigue syndrome

EDITOR,—Michael Sharpe and colleagues' paper confirms what many clinicians have long suspected—namely, that the prognosis for those with a chronic fatigue syndrome who reach specialist care is poor.¹ The paper also suggests that membership of a self help organisation is associated with a poor outcome. Although the authors emphasise that this association is not necessarily causal, I fear that the self help organisations may interpret this as another attack on their credibility, which will further sour relations between the organisations and the profession.

What are the possible explanations for these disturbing findings? Sharpe and colleagues suggest that patients' beliefs are an important mediator of disability, a view I share.² An article written by a sufferer illustrates how this might happen: "These living viruses are erratic and unpredictable. The prickly-edged ones pierce their way into the body cells. If disturbed by the patient's activity they become as aggressive as a disturbed wasps' nest, and can be felt giving needle-like jabs (or

stimulating the nerves to do so)."³ It is easy to understand how such beliefs, regardless of their scientific accuracy, amplify disability.

The situation is rendered more tragic as it now seems that the evidence on which these beliefs (that persistence of enteroviruses in muscles is the cause of undoubtedly genuine symptoms) is based is less than convincing. Previous work on enteroviral serology is now known to be unreliable,⁴ as is the finding of persistent enteroviral antigenaemia.⁵ Most importantly, it seems increasingly unlikely that this condition results from any neuromuscular disorder, viral or otherwise.⁶ I hope that this more optimistic research will be publicised with the same vigour that greeted previous findings.

Sharpe and colleagues' findings of a poor prognosis should cause all those who advise patients with the chronic fatigue syndrome to pause for thought and perhaps discard cherished beliefs. Members of the medical profession should also rethink their attitudes towards sufferers as, clearly, neither the profession nor the self help organisations are effective at relieving disability.

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- 1 Sharpe M, Hawton K, Seagroatt V, Pasvol G. Follow up of patients presenting with fatigue to an infectious diseases clinic. *BMJ* 1992;305:147-52. (18 July.)
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EDITOR,—Michael Sharpe and colleagues' follow up study of 177 patients with chronic fatigue of uncertain origin raises several important unanswered questions, which require further investigation.¹ Factors such as a belief that their illness followed an infection, intolerance to alcohol, and membership of a support group for patients with myalgic encephalomyelitis were all associated with an adverse prognosis. Could it be that the authors had identified patients belonging to a distinct postinfectious subgroup as many doctors maintain they do? Clearly, if this is the case future studies of this nature will have to include more objective analysis of persisting viral infection (for example, analysis of muscle biopsy specimens with the polymerase chain reaction rather than tests for VP1 antigen); immune function (for example, function of natural killer cells rather than white cell counts); and hypothalamic-pituitary-axis activity (for example, up regulation of serotonin-1 receptors and basal cortisol concentrations) to see if there are characteristic abnormalities that distinguish the postinfectious subgroup.

The high incidence of intolerance to alcohol is noted as intriguing, but from personal experience, as well as from seeing many patients with a classic postinfectious fatigue syndrome, I regard this observation as an important diagnostic feature. In these patients even small amounts of alcohol cause a further deterioration in cognitive function, and I suggest that a physiological explanation may lie in the fact that alcohol increases the concentration of the neurotransmitter γ -aminobutyric acid, which in turn reduces the availability of calcium ions and hence depresses brain function still further.²

The observation that four of 55 patients had greatly improved, and a further 13 were worse, as a result of antidepressant treatment also brings into question Sharpe's recent conclusion "that such patients may be suffering from a depressive

illness, of which physical fatigue is a somatic manifestation."³ Although these drugs clearly have a role in patients with coexistent depression, a much larger survey of 336 patients found that, overall, they were no more effective than therapeutic nonsense such as a regimen to eliminate candida.⁴

The problem with any kind of research into the chronic fatigue syndrome is that, like backache, it covers a large heterogeneous group of patients in whom physical, psychological, and social factors may be interacting. Researchers should therefore not be surprised to find that the outcome varies considerably when the aetiology is not more clearly defined.

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- 1 Sharpe M, Hawton K, Seagroatt V, Pasvol G. Follow up of patients presenting with fatigue to an infectious diseases clinic. *BMJ* 1992;305:147-52. (18 July.)
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- 3 Wood C, Magnello ME, Sharpe MC. Fluctuations in perceived energy and mood among patients with chronic fatigue syndrome. *J R Soc Med* 1992;85:195-8.
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EDITOR,—Michael Sharpe and colleagues report that most patients with the chronic fatigue syndrome rate contact with medical services as unhelpful or only slightly helpful.¹ Many sufferers turn to alternative health care, again with varied success. Such dissatisfaction with medical care is well documented,² and self help organisations flourish to provide the support, advice, and education that is not, or cannot be, provided by the medical profession; they potentially fulfil an important role.

The authors conclude that for patients with the chronic fatigue syndrome membership of a self help organisation is associated with a poorer outcome (although whether members were more functionally impaired at the outset is not known). Adopting coping strategies, particularly with regard to exercise and "stress," and a belief in the persistence of a viral infection are also associated with continuing disability.

Unfortunately, such advice continues to be offered to patients with the syndrome, particularly by self help organisations. It is to be hoped that all those caring for patients will take note of Sharpe and colleagues' conclusions. Work with fatigued patients in primary care (E McDonald *et al*, paper in preparation) suggests that general practitioners have a central role in preventing the longer term secondary disability described by the authors—by acknowledging the distress caused by fatigue, limiting investigations and referrals to specialist centres, prescribing antidepressants when appropriate, and encouraging maintenance of activities. The patients in Sharpe and colleagues' study were receiving secondary care, and possibly by then beliefs and attitudes to physical symptoms are already engrained.

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- 2 David AS. Postviral fatigue syndrome and psychiatry. *Br Med Bull* 1991;47:966-88.

Dangers of aspirin before cardiac surgery

EDITOR,—In the final paragraph of his editorial Stuart M Cobbe states, "The outcomes of ISIS-3 and GISSI-2 have resulted in a policy of no change and a sigh of relief from most British doctors and

general managers. Aspirin and streptokinase remain the treatment of choice in myocardial infarction; there seems little justification for adding heparin.¹ This is not good news for those patients who, after myocardial infarction, have to proceed to urgent or semiurgent cardiac surgery for unstable angina or other aspects of the infarction.

The effect of aspirin on platelets results in difficult and sometimes uncontrollable and fatal bleeding. Cobbe's conclusions are not good news for cardiac surgeons or managers or for patients if they have to sit around in hospital for several days waiting for "urgent" surgery for their unstable angina while the effects of the aspirin wear off. Nor is this good news for the cardiologists, cardiac surgeons, and haematologists who have to decide when it is safe to operate.

I have two questions. Firstly, is it not possible to use a non-steroidal anti-inflammatory agent other than aspirin which would have a similar effect on platelets but a much shorter half life so that cardiac surgery could proceed safely within 24 hours of the drug being stopped? Secondly, could members of the British Cardiac Society and the British Society of Thoracic and Cardiovascular Surgeons produce guidelines on this contentious aspect of cardiac surgery?

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1 Cobbe SM. ISIS 3: the last word on thrombolysis? *BMJ* 1992;304:1454-5. (6 June.)

AUTHOR'S REPLY.—It is important to emphasise that only a small minority of patients who have received thrombolytic treatment for acute myocardial infarction require cardiac surgical intervention. In the few patients with persisting unstable angina after myocardial infarction, withdrawal of aspirin before coronary artery bypass grafting may increase the risk of acute coronary occlusion and reinfarction. As a result of this the cardiac surgeons in this hospital undertake coronary bypass grafting on such patients without stopping aspirin. Their recent study indicated that the median post-operative blood loss was increased by 490 ml in patients receiving 150 mg of aspirin compared with controls.¹ This was associated with a median increase in the transfusion requirement of two units of red cell concentrates, and fresh frozen plasma, platelets, or cryoprecipitate were required in 20% of patients treated with aspirin compared with 5% of controls ($p < 0.01$). There was no increase in the median postoperative hospital stay.

Use of other non-steroidal anti-inflammatory drugs has not been validated in terms of their effect on mortality after myocardial infarction. Furthermore, experimental studies suggest that these drugs may impair the healing of an infarct and lead to its expansion and an increased risk of cardiac failure.²

I do not disagree with Holden's view that aspirin increases bleeding after coronary bypass grafting. In my view, the small risk of excess surgical bleeding associated with aspirin has to be accepted as the price to be paid for avoiding preoperative coronary occlusion in the small proportion of patients who develop unstable angina after thrombolytic treatment for acute myocardial infarction. These considerations should not be allowed to detract from the clear benefit associated with treatment with aspirin.

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1 Taggart DP, Siddiqui A, Wheatley DJ. Low-dose preoperative aspirin therapy, postoperative blood loss, and transfusion requirements. *Ann Thorac Surg* 1990;50:425-8.

2 Jugdutt BI. Delayed effects of early infarct-limiting therapies on healing after myocardial infarction. *Circulation* 1985;72: 907-14.

Diarrhoea, dysentery, and food poisoning

AUTHOR'S REPLY.—J K Anand raises a valid point. My intention, however, was to point out the role of notification and control of infection in the overall management of infectious diarrhoea and not to discuss specific cases. Owing to the similar presentation of many of these diseases, I consider barrier nursing prudent for patients with these diseases on admission to hospital pending a firm microbiological diagnosis. After diagnosis the infection control procedure can be reviewed and revised—hence the need to consult the local infection control policy, as I stated in my letter.

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AUTHOR'S REPLY.—J K Anand raises a valid point. My intention, however, was to point out the role of notification and control of infection in the overall management of infectious diarrhoea and not to discuss specific cases. Owing to the similar presentation of many of these diseases, I consider barrier nursing prudent for patients with these diseases on admission to hospital pending a firm microbiological diagnosis. After diagnosis the infection control procedure can be reviewed and revised—hence the need to consult the local infection control policy, as I stated in my letter.

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Selective serotonin reuptake inhibitors

EDITOR.—In his editorial on selective serotonin reuptake inhibitors J Guy Edwards presents a conservative view of the current situation with regard to the prescription of antidepressants.¹ He comments that "those recently marketed in Britain include fluvoxamine, fluoxetine, sertraline, and paroxetine." Fluvoxamine has been available since 1987 and fluoxetine since 1989. He rightly states that in terms of efficacy selective serotonin reuptake inhibitors are not superior to tricyclic antidepressants, but the profile of their side effects does offer advantages for patients.

Edwards says that "clinical anecdotes . . . do not provide good evidence of cause and effect" yet reports several single cases of adverse reactions. He mentions that prescription event monitoring showed that 24 women had become pregnant while taking a selective serotonin reuptake inhibitor but does not state at what point the pregnancy occurred. None of these drugs is recommended in pregnancy, but patients commonly become pregnant during treatment.

With particular reference to fluoxetine Edwards makes an erroneous statement—that six weeks is required before treatment with a monoamine oxidase inhibitor is started. The datasheet states that at least five weeks should elapse.

I believe that many psychiatrists would take issue with Edwards over his suggestion that the "main uses of selective serotonin reuptake inhibitors would seem to be in clinically depressed patients who are unable to tolerate tricyclic antidepressants and those with associated troublesome obesity or heart disease." The selective serotonin reuptake inhibitors have been an enormous advance not only in the treatment of depression but in developing the understanding of other disorders such as anxiety, panic disorder, obsessive compulsive disorder, and bulimia nervosa.

Disappointingly, Edwards concludes with a price comparison and the comment, "Whether they are worth the extra cost is something that

individual doctors and patients will have to decide." It sounds as though Edwards has already made up his mind, which presumably also means that of his patients.

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1 Edwards JG. Selective serotonin reuptake inhibitors. *BMJ* 1992;304:1644-6. (27 June.)

EDITOR.—If there are two classes of drug that are equally effective in treating depression, one of which is cheap but highly toxic and the other of which is safe but perceived to be expensive, a doctor cannot decide between the two on economic grounds. This ethical crisis, however, faces general practitioners daily when balancing their patients' welfare.

I believe that it is only a matter of time before a general practitioner is asked to defend himself or herself, in a civil suit brought by relatives of a patient who has committed suicide, against charges of having negligently provided that patient with the means to commit suicide. If I was that general practitioner and I had not at least tried one of the newer selective serotonin reuptake inhibitors I would find it difficult to defend my position. The process of litigation is exceedingly slow, and by the time such a case was resolved there would be thousands more in the pipeline.

J Guy Edwards, I believe, has overlooked these overwhelming moral and economic reasons why we should have professional agreement that tricyclic antidepressants are no longer acceptable as first line antidepressant treatment.

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Adrenaline in allergic emergencies

EDITOR.—We think that G B Smith and B L Taylor's comments on the treatment of allergic emergencies¹ in reply to our original letter² are misleading. They conclude that "when adrenaline is required in an anaphylactic emergency it should be given . . . intravenously." We are concerned about the implications of such a recommendation. Firstly, it is contrary to current recommendations in the *British National Formulary*.³ In the section on allergic emergencies (section 3.4.3) in the formulary the use of adrenaline is emphasised: "IMPORTANT. Intravenous route is for cardiac resuscitation only." In the section on sympathomimetics (section 2.7) it is similarly emphasised: "IMPORTANT. For acute anaphylaxis use intramuscular route."⁴

Smith and Taylor say that "vasodilatation is a major pathophysiological characteristic of anaphylaxis," but this is not always the case, and venous access can be difficult, particularly outside hospital. Furthermore, intravenous adrenaline has been reported to lead to serious adverse reactions, and this concern cannot just be dismissed by the statement, "Concerns for the potential dangers . . . are largely misfounded." This is particularly relevant as there are only limited reports on its use other than to point out the problems encountered with intravenous administration.⁴ Smith and Taylor's conclusion may result in a trend towards intravenous administration of adrenaline in allergic emergencies without due consideration of the potential hazards.¹

In conclusion, we do not entirely disagree with