

When the potential side effects of physical therapy (such as dependency) and the cost are taken into account there is not enough evidence to promote the maintenance of physical activity in the acute phase of low back pain.

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## Use of interferon beta 1b for multiple sclerosis

### Patients will put up with side effects because of their desire to beat the disease

EDITOR,—As a physician who has both multiple sclerosis and a doctorate in clinical pharmacology, I am probably in a unique position to answer Peter Harvey's question of why interferon beta 1b was licensed.<sup>1</sup>

Multiple sclerosis, particularly the relapsing-remitting form, is a notoriously difficult illness on which to perform clinical trials. This probably accounts for the large number of initially promising treatments that later proved to be useless. To my knowledge, interferon beta 1b is the only treatment that has been shown to have a significant beneficial effect on multiple sclerosis in large randomised controlled trials. If one reads the results of the trials carefully (as Harvey obviously has) it is apparent that the drug is not the panacea that the popular press would lead us to believe that it is. It also has unpleasant side effects. These are the reasons why I do not take it myself. Its development and the trial methods, which used magnetic resonance imaging, have, however, led to hope of better treatments to come and better ways of evaluating them.

Harvey has not taken into account another important factor, which is the desperate desire of people with multiple sclerosis (and their families) to do something to treat the disease. This desire becomes especially strong during an acute relapse. Unless something better is discovered before then, I will probably end up taking interferon beta 1b after my next bad relapse.

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- 1 Harvey P. Why interferon beta 1b was licensed is a mystery. *BMJ* 1996;313:297-8. (3 August.)

### Manufacturer defends the drug

EDITOR,—It was disappointing to read Peter Harvey's letter dismissing the value of interferon beta 1b in the treatment of patients with relapsing-remitting multiple sclerosis.<sup>1</sup> Harvey takes no account of the results of controlled clinical trials showing a significant reduction in severity and frequency of relapses (up to 30-50%),<sup>2,3</sup> with the most severe cases benefiting most, or of the accumulating data showing that generally there is a reasonable correlation between findings on magnetic resonance imag-

ing and clinical status.<sup>3-5</sup> Individual cases do not render the overall evidence invalid.

Harvey fails to recognise that a reduction in the frequency and severity of attacks can make an immense difference to the quality of life of a patient with multiple sclerosis. It can mean the difference between being able to work or not, being able to go shopping or not, and between independence or reliance on others. To dismiss these improvements as inconsequential does a disservice to both patients and the drug.

While it is true that some patients experience side effects, such as flu-like symptoms in the first few weeks of treatment, simple measures can be taken to minimise this; in our experience the dropout rate due to side effects in the first six months of treatment is of the order of only 3%. The issue of neutralising antibodies is not a simple one as suggested by Harvey, and antibody titres do not correlate strongly with a reduction in the drug's effectiveness. Above all, it must be a clinical judgment whether an individual patient should continue treatment, depending on the benefit received.

As clinical experience with interferon beta 1b increases I hope that those who adopt polarised positions will come to modify them. In the meantime, Schering will put the evidence forward by whatever means possible, including in the *BMJ*; this is especially important when contacts of any kind with the company are spurned, as in Harvey's case. It is patients who stand to suffer by being denied an effective treatment.

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- 1 Harvey P. Why interferon beta 1b was licensed is a mystery. *BMJ* 1996;313:297-8. (3 August.)
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### Importance of relapses must not be underestimated

EDITOR,—Peter Harvey asserts that patients with multiple sclerosis are interested in disability and, by implication, are not interested in relapses.<sup>1</sup> While many patients with multiple sclerosis cope successfully with relapses, for a considerable proportion of patients relapses are frequent and severe, causing great distress and disruption to normal life. It is strange to condemn the first licensed product to show an effect on relapses because it has not also been shown to affect disability without acknowledging the importance of relapses in patients' lives.

Equally, it is rather negative to place so much emphasis on the side effects of this drug without giving equal weight to the potential benefits. Experience even before the product was licensed in 1995 shows that patients with multiple sclerosis are capable of weighing the evidence on treatments and reaching rational conclusions; hence the lack of the feared stampede for interferon beta 1b. The Multiple Sclerosis Society has put great effort into ensuring that the evidence has been available to patients in a balanced and intelligible form and has looked to doctors to do likewise.

Harvey's view is incapable of defence without better evidence than anecdote from the narrow context of the clinic. In Britain the shortage of neurologists means that few neurologists can afford extensive contact with their patients with multiple sclerosis, and the waiting times for outpatient appointments and admissions ensure that patients are rarely seen by their consultant during an exacerbation. It is not surprising, therefore, that the importance of relapses to patients is often underrated by British neurologists, and this may go some way to explaining the differences in levels of prescribing of interferon beta 1b between Britain and other countries.

Harvey falls into the same trap as the authors of the landmark studies of interferon beta<sup>2,3</sup> in making assumptions about the treatment priorities of patients with multiple sclerosis. In the context of carefully designed, multimillion dollar clinical trials it seems strange to those of us in daily contact with large numbers of patients that neither investigators nor pharmaceutical companies have sought firm evidence on this. Given the current range of possibilities, would patients with multiple sclerosis prefer their relapses to be treated or not? This is an important issue that has not yet been investigated, even though further costly large scale trials continue to be advocated. The Multiple Sclerosis Society is interested in potential collaborations on this question and would be pleased to hear from others of like mind.

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- 1 Harvey P. Why interferon beta 1b was licensed is a mystery. *BMJ* 1996;313:297-8. (3 August.)
- 2 IFNB Multiple Sclerosis Study Group. Interferon beta-1b is effective in relapsing-remitting multiple sclerosis. Clinical results of a multicenter, randomised, double-blind placebo-controlled trial. *Neurology* 1993;43:655-61.
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## Practice in endoscopic cholangiopancreatography in Denmark differs from that in Britain

EDITOR,—Jacob Rosenberg and colleagues' conclusion that premedication with metoprolol prevents myocardial ischaemia during endoscopic cholangiopancreatography has important implications for routine technique in this procedure.<sup>1</sup> The applicability of this finding to current clinical practice in Britain, however, is unclear since there are considerable differences between the British Society of Gastroenterology's guidelines and the practice in this Danish study.<sup>2</sup>

In the study group patients did not receive preoxygenation with supplemental oxygen, morphine rather than pethidine was used as the opiate, and larger doses of hyoscine bromide were used than is common in Britain. The use of lignocaine spray in heavily sedated patients is also contrary to the British Society of Gastroenterology's advice. The high incidence of myocardial ischaemia (53%) and the presence of myocardial infarction in the relatively small group of 19 patients treated with placebo suggests that placebo conditions may have been substantially suboptimal. Continuous monitoring of blood pressure during endoscopic cholangiopancreatography is currently not routine in many centres in Britain but would clearly be necessary if premedication with a  $\beta$  blocker was used.

The study highlights the importance of tachycardia and illustrates the risk of myocardial ischaemia, but further data will now be required to determine whether premedication with metoprolol improves safety in patients receiving

supplementary oxygen who are monitored by routine oximetry and given conventional sedation. Until this information is available, routine use of a  $\beta$  blocker for patients undergoing endoscopic cholangiopancreatography seems premature because the risk of hypotension induced by  $\beta$  blockade may be an additional hazard.

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## Danish data confirm low prevalence of HRT among women prescribed oral corticosteroids

EDITOR,—L J Walsh and colleagues report the use of oral corticosteroids in a population of 65 786 in Nottinghamshire.<sup>1</sup> They had found few epidemiological data on the use of corticosteroids in community populations, which is surprising, since the potential side effects of corticosteroids—for example, osteoporosis, hypertension, and diabetes—are important.

We report here supplementary data on the use of oral corticosteroids and hormone replacement therapy obtained from a population based prescription registry for the county of North Jutland in Denmark. The region has 330 general practitioners and 487 000 inhabitants. For each prescription for drugs for which the costs are reimbursed the pharmacies collect the name and amount of the drug, the defined daily dose, the personal registration number of the patient, the date that the drug is dispensed, and several other variables.

The population consisted of 242 614 men and 244 379 women. In the database we identified 3023 men (1.2%) and 4133 women (1.7%) who had received at least one prescription for oral corticosteroids in 1993. Walsh and colleagues found that 0.5% of their population had been "continuously" treated with oral corticosteroids. The difference is probably due to the different inclusion criteria, as Walsh and colleagues included only patients treated with oral corticosteroids for at least three months. Among the 4133 women who had received corticosteroids in North Jutland we identified 567 (13.7%) who had received hormone replacement therapy. In their study Walsh and

colleagues found that 14% of the women treated with corticosteroids had received hormone replacement therapy.

The incidence of the most common conditions requiring continuous treatment with oral steroid increases with age. Correspondingly, we found that the proportion of the population treated with steroids increased with age (table 1).

Steroid treatment increases the risk of osteoporosis and fractures,<sup>3-5</sup> and prophylactic treatment for osteoporosis should certainly be considered when steroids are prescribed. We do not know the proportion of patients who had received advice on diet, exercise, or over the counter drugs to help prevent osteoporosis, but we find the proportion of women who received hormone replacement therapy surprisingly low, given the strategies recommended for preventing fractures caused by steroid induced osteoporosis.<sup>2</sup>

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## Investigation is needed into why some patients are not offered cardiac rehabilitation

EDITOR,—Jill Pell and colleagues report the influence of social deprivation on the uptake of cardiac rehabilitation.<sup>1</sup> Through their study the authors have identified an important area of research that could eventually lead to improvements in rehabilitation for deprived patients. In 1995 we reported that economically disadvantaged patients showed poorer survival than others after myocardial infarction,<sup>2</sup> and Pell and colleagues' study suggests a possible mechanism for this: that fewer deprived patients take up and complete rehabilitation programmes.

We note that the type of consultant and the hospital attended were also associated with

uptake of rehabilitation. Just as striking is that the invitation to take up rehabilitation also depended on the consultant and hospital attended. In addition to carrying out research into why deprived patients are less likely to complete rehabilitation we clearly need to ask ourselves why some patients are not invited in the first place. The sizes of the effects suggest that the potential for improvement lies as much with the medical community as with the patients.

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## People will be able to surf across languages for health data on the Internet

EDITOR,—Health research data and other health data are increasingly stored in electronic format on networks, which enables faster and more flexible access to the literature. One of the most widely used on line databases in the health field is Medline, which contains more than 7.5 million citations from over 4000 biomedical journals and is international in scope. Increased access to the Internet will further facilitate worldwide distribution of health information. The Internet currently reaches an estimated 40 million people in 90 countries, and the number of its host computers is expected to exceed 100 million before the year 2000.

Language barriers serve to block the globalisation of health information resources. Although English is widely used in science, not everyone can communicate well in English. Much useful information in web sites on the Internet is in languages other than English. Only a few home pages that are in languages other than English provide abstracts in English. This restricts the sharing of information worldwide.

To help globalise health information further we are setting up a multilingual home page for the global health network (<http://www.pitt.edu/HOME/GHNet/GHNet.html>) on the Internet.<sup>1,2</sup> The first step is to translate the English version into other languages so that more researchers and practitioners can use the home page in their mother tongue (a Japanese version is at <http://www.pitt.edu/HOME/GHNet/GHNet-j.html>). The second step is to build a home page dealing with health information available from countries where the home page is not in English. The third step will be to put a short description about the site, in English, into each foreign language site along with the email address of a person in charge of the site who can communicate in English. That person will serve as a contact when English speaking people access the site. Finally, we will either include computer assisted translation software among our site services or link our site to others providing such services. Such software now can provide a rough but usable translation, and its quality will improve in the coming years.

Table 1—One year prevalence of treatment with oral corticosteroids in North Jutland, Denmark, by age

Age (years)	No (%) who had received corticosteroids		No (%) of women who had received HRT*
	Men	Women	
0-29	172/99 417 (0.2)	224/93 087 (0.2)	37 (16.5)
30-39	212/35 204 (0.6)	268/33 710 (0.8)	43 (16.0)
40-49	337/36 613 (0.9)	462/34 918 (1.3)	68 (14.7)
50-59	380/26 405 (1.4)	567/26 567 (2.1)	78 (13.8)
60-69	646/21 835 (3.0)	858/23 964 (3.6)	99 (11.5)
70-79	845/16 282 (5.2)	1071/20 130 (5.3)	143 (13.4)
80-89	396/6162 (6.4)	594/9090 (6.5)	85 (14.3)
≥90	35/694 (5.0)	89/1573 (5.7)	14 (15.7)
Total	3023/242 614 (1.2)	4133/24 4379 (1.7)	567 (13.7)

HRT = Hormone replacement therapy.

\*Women who had received at least one prescription for corticosteroids.