Post-marketing surveillance of enalapril

Sir,

We would like to comment on the post-marketing surveillance study of enalapril by Cooper and colleagues (August *Journal,* p.346). In this study serious adverse reactions occurred in 0.5% of patients treated and 4.2% withdrew from the study because of adverse events. The patients in this study were a selected population with uncomplicated essential hypertension who would be expected to be at low risk of developing adverse reactions. In a less favourable clinical situation a higher incidence of serious adverse reactions might be expected. However, the paper makes no mention of the reported data of the Committee on Safety of Medicines reflecting general clinical use, and it fails to discuss the important changes made to the data sheet for enalapril during the course of the study.

During the first year of marketing it became evident from yellow card reports received by the Committee on Safety of Medicines that severe hypotension, renal failure and angioneurotic oedema could occur when enalapril was used to treat hypertension or congestive cardiac failure. As a consequence, the Committee considered it necessary to make major changes to the therapeutic indications, dosage and treatment precautions for the drug. Merck, Sharpe and Dohme were in agreement and letters were sent to all doctors in January and March of 1986 informing them of the changes. These were reiterated in May 1986 in *Current Problems*[1] where it was advised that:

1. Enalapril should be used as a second line agent in the treatment of hypertension when standard therapy is ineffective or contraindicated because of adverse effects.
2. When used as an adjunctive therapy in the treatment of congestive cardiac failure, treatment with enalapril should always be initiated in hospital under close supervision.
3. The recommended starting dose for all patients with congestive cardiac failure and all those over 65 years of age has been reduced to 2.5 mg per day. For hypertension, a starting dose of 5 mg per day is now recommended in patients under 65 years of age.
4. The dose of any diuretic being given concurrently should be reduced before initiating treatment with enalapril, where this is feasible.
5. Renal function should be monitored in all patients before initiation of treatment and during treatment, when appropriate. The drug should be used cautiously in any patient with renal impairment.

In important respects the findings of Cooper and colleagues differ from those of the Drug Safety Research Unit[2] and from the experience of the Committee on Safety of Medicines' drug monitoring scheme. Doctors should therefore be aware that unacceptable serious adverse reactions may occur unless the precautions given in the current data sheet for enalapril are observed.

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References

1. Committee on Safety of Medicines. Adverse reactions to enalapril (Innovace). *Current Problems* 1986; 17.
2. Drug Safety Research Unit. 'Innovace' (enalapril). *PEM News* 1987; **4**: 6-13.

Sir,

I was most interested to read the editorial and paper on post-marketing surveillance (August *Journal,* p.337, 346). However, as one who has worked full-time in the pharmaceutical industry and now retains industry links from general practice, I believe that the issues arising are wider than the specific issue of post-marketing surveillance.

First, general practitioners should be more accountable for their prescribing and more knowledgeable and interested in the details of the particular drugs they choose. Detailed evaluation of individual drugs is a complicated and time consuming business and in general I think we should be more willing to participate. Secondly, it is important that the pharmaceutical industry avoids taking a short term sales oriented view of drug evaluation in general practice. Thirdly, a responsibility falls upon journals like this to take a lead with publication and I would hope that these articles are just the beginning of a greater involvement in the publication of suitable papers arising from cooperation between doctors and the pharmaceutical industry.

In the past the reputation of general practice drug trials has been poor. There are initiatives to improve the quality of work relating to the use of drugs in general practice and I hope the publication of drug trials as well as post-marketing surveillance will help establish a more harmonious and acceptable relationship between general practitioners and the pharmaceutical industry.

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MRCGP examination

Sir,

While there is some merit in the suggestion that the MRCGP exam should be in two parts, Dr Seiler's idea that the first part could be shared with part one of the MRCP seems inappropriate (July *Journal,* p.323).

The College recommends that trainees should learn about conditions which are common, acute or life threatening, chronic illnesses and those where early detection may minimize possible complications.[1] If the College adopted Dr Seiler's suggestion candidates would have to acquire knowledge which would be superfluous to them in general practice and there would be fewer entrants for an examination seen to be increasingly irrelevant.

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Reference

1. Royal College of General Practitioners. *The future general practitioner.* London: British Medical Journal, 1972.

Research methods course

Sir,

I wish to draw attention to the recent residential course held at Nottingham University on 9–12 September entitled 'Research methods and design in general practice'. The course was expertly planned and was of equal benefit to the young general practitioner with an idea he would like to research and the older doctor who has already embarked upon research.

For those who missed the course and have a research idea I would recommend a visit to the local department of general practice for discussion with someone who may be able to structure their thinking and planning in an appropriate direction.

For those able to plan that far ahead, the next research methods course will be held in Bristol in 1988 and I would commend it to any general practitioner with a questioning mind.

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