selected new drug during a particular period of observation. The scheme is notified by the Prescription Pricing Authority of every prescription of the drug, and after a time sends a form to the prescriber, asking for notification of any adverse events reported by the patient to them. About half the cards sent out are returned. The collected data for a specific drug and event are used to calculate incidence density (the ratio of the number of reports of the event during treatment to the number of patient-months of exposure to the drug).² The relative risk of a given event across a group of drugs is estimated by comparing incidence densities.

The observational studies are, of course, not randomised and so may be biased.³ For example, one preparation may be particularly used for a specific condition or age group, or there may be differential failure to detect, record, or report an adverse event. Estimates should be viewed with circumspection even if bias seems unlikely—several incidence ratios for many different events can be examined, and some will inevitably differ from others because of random variation. The associated significance will be misleading unless correction has been made for multiple comparisons. Results also have to be set in clinical context. We should certainly be reassured by the low overall incidence of sedation with selective histamine H₁ antagonists shown by Mann et al: fewer than one

patient in 140 complained of drowsiness with any of these drugs. There are some differences between them, which may be relevant to people in safety critical jobs.

As the authors point out, the investigation would not have been possible without the cooperation of the reporters, who should be encouraged by seeing that their efforts are worth while. In due course, computerised systems such as the general practice research database may allow post-marketing surveillance without tears.^{4,5} Until then, we will all benefit from the information that diligent reporters send on yellow cards and green forms.

Competing interests: The West Midlands Centre for Adverse Drug Reaction Reporting receives financial support from the Medicines Control Agency.

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A memorable patient

Keep looking for a reason

Sarah was 22 when she presented with the dreadful signs of a large space-occupying lesion deep in the dominant parietal lobe. She was drowsy with a severe headache, had severe dysphasia, and there was a significant rightsided weakness. The computed tomography said it all; a malignant intrinsic tumour at the trigone of the lateral ventricle, probably a glioblastoma.

She rallied a little on steroids overnight and so I performed a craniotomy, having suitably warned her worried family of the likely outcome and prognosis. I found a very bloody tumour that had some definition from the surrounding brain. The pathologist told me that the frozen section showed a highly malignant brain tumour, consistent with the radiologist's diagnosis.

The survival from this type of tumour in this position is measured in months, and there is no evidence that surgery does much more than relieve the pressure symptoms. Consequently, I completed a cautious internal decompression, stopped the bleeding, and closed up. She was unchanged, but bled into the tumour remnant the following day and I had to reopen the craniotomy. That night I was relieved that she was no worse.

Sarah's tumour was a gliosarcoma. This is a rare and even more malignant variant of a glioblastoma, in which it is thought that the new vessel forming factors released by the primary brain tumour induce sarcomatous change in the blood vessels. The news was not good.

Surprisingly, Sarah started to get better. Her speech improved and her hemiparesis almost disappeared. She was referred for radiotherapy and underwent the full six weeks' course. The follow up scan also looked good. She lost her job in insurance, but became a police receptionist.

Two years went by, but there was no sign of the tumour on further scans. By then, Sarah had become a good friend of the hospital, active in collecting money for the development fund, and talking to the press about her treatment.

After three years, when the vast majority of patients with a glioblastoma are dead, I asked the pathologists to review the case,

but despite the tumour's unusual behaviour, they could not come up with any other diagnosis.

Meanwhile, Sarah had married and was thinking of starting a family. By this time, much more sensitive magnetic resonance imaging had become more freely available, and the scan showed no recurrence. At six years, I asked the pathologist to rereview the case. By now, immunocytochemistry was much more sophisticated, and despite the mitoses and other seemingly malignant features, he was able to reclassify the lesion as a much more benign pleomorphic xanthoastrocytoma.

When I told Sarah this exciting news, I was most surprised that it seemed unimportant to her, almost to the point of disinterestedness.

She remains well almost 10 years from diagnosis. Her scan is clear, but she still worries about recurrence. I worry about the possibility of radionecrosis which sometimes afflicts long term survivors of brain irradiation.

I have learnt three things from Sarah's case. Firstly, that having lived with the diagnosis of having had cancer but being free from recurrence, being an unusual statistic with a semibenign condition of unknown behaviour lacks meaning. Secondly, when tumours behave in highly unusual ways, keep looking for a reason. Thirdly, do not expect other patients' tumours to behave in a similarly unusual fashion—a temptation that I fell into at least once.

Michael Powell consultant neurosurgeon, London

We welcome articles of up to 600 words on topics such as *A memorable patient*, *A paper that changed my practice*, *My most unfortunate mistake*, or any other piece conveying instruction, pathos, or humour. If possible the article should be supplied on a disk. Permission is needed from the patient or a relative if an identifiable patient is referred to. We also welcome contributions for "Endpieces," consisting of quotations of up to 80 words (but most are considerably shorter) from any source, ancient or modern, which have appealed to the reader.