Cassileth *et al*, who explored the relation between patients' early recognition of superficial spreading melanoma and depth of invasion,[1] provide no support for a direct correlation between time to excision of the primary lesion and tumour thickness.

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Diuretic treatment in decompensated cirrhosis and congestive heart failure

SIR,—Dr Helmer Ring-Larsen and others (24 May, p 1351) suggest that the blunted renal response to a diuretic agent in the upright as compared with the supine position is due to the activation of several hormonal mechanisms. They found evidence for increased activity of the sympathetic nervous system and of the renin-aldosterone axis and mention vasopressin as another important homoeostatic measure. However, they do not consider the possible role of the atrial natriuretic factor.

Several observations indicate that this novel diuretic and natriuretic peptide[1] has a substantial role in volume homoeostasis. We and others have shown that patients with hypertension or congestive heart failure show greatly increased plasma concentrations of atrial natriuretic factor, which are well correlated with right atrial pressures.[2,3] In patients with cirrhosis we showed that discontinuation of diuretic treatment could increase circulating concentrations of atrial natriuretic factor.[4] Values in children with renal insufficiency are greatly increased and correlate well with the degree of volume expansion; they are significantly reduced after volume reduction by haemodialysis.[5] Changes in posture influence plasma atrial natriuretic factor values.[6] In the supine position central venous and right atrial pressure increase due to volume shifting. Such an increase, induced by head out water immersion, has been shown to stimulate release of atrial natriuretic factor in healthy subjects[7] and in patients with cirrhosis.[8]

These findings support the contention that atrial natriuretic factor is an important factor in volume regulation in health as well as disease. Determination of atrial natriuretic factor concentrations might be useful in studies of volume regulation and might elucidate the still unresolved complex of posture dependent diuresis.

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Non-steroidal anti-inflammatory drugs and serious gastrointestinal adverse reactions

SIR,—The CSM update (3 May, p 1190) is a useful method of approximating the relative risks of non-steroidal anti-inflammatory drugs and will no doubt be widely quoted. However, the data for fenbufen contain an error in that the number of prescriptions stated has been miscalculated.

Prescription numbers obtained from the DHSS office of statistics for the time period covered in the review should have been 1·97 million and not 1·57 million as shown. Fenbufen tablet prescriptions for 1984 have been inadvertently omitted. Consequently I believe that table II should read (deaths in parentheses):

Gastrointestinal reactions per million prescriptions	28·4 (1·5)
Other serious reactions per million prescriptions	26·9 (2·0)
Total serious reactions per million prescriptions	55·3 (3·6)

Although these changes do not radically alter the general interpretations in this article, I am anxious for these corrections to be published because this useful review will no doubt become a much used reference source.

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CSM'S REPLY—We acknowledge the error in the fenbufen data pointed out by Dr Cohen. We wish to emphasise that prescribers should not use differences in the reporting rates among drugs in the second group of table II as a guide to the relative safety of this group of drugs. In terms of overall safety these drugs cannot at present be clearly distinguished from each other on the basis of this analysis of yellow card reports.

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Laboratory equipment

SIR,—I was dismayed by Dr B J Boughton's flippant and cynical attitude in his Personal View (24 May, p 1986). Fortunately most pathologists are more responsible in their efforts to acquire the tools of their trade. At least Dr Boughton can sit on a committee where resource allocation is openly discussed. This was also my experience as a senior lecturer at King's College Hospital (South East Thames region), but here the North Western region makes its decisions by a secret cabal in Manchester. This system was devised years ago by canny Mancunians, who perceived the disadvantages in the RAWP principle and have ensured that the bulk of money for equipment stays in central Manchester.

The problem here is further compounded by a disastrous new regional policy to cut the medical equipment budget by 15% before 1993. Dr Boughton would doubtless approve of this scheme and volunteer his own laboratory not to replace its Coulter counter (bought by a predecessor) when it becomes too expensive to maintain (although never worn out, of course). Since he knows that "laboratory tests are almost useless" he could no doubt use his Neubauer counting chamber for his patients receiving chemotherapy for leukaemia or lymphoma, whose white cells or platelets need to be counted from time to time.

Virtually all consultants, regardless of specialty, need sophisticated equipment to enable them to practise modern medicine. So far the NHS has quite failed to keep pace with technology because of its expense. Dr Boughton's plea for nostalgia (to be polite) may please his hard pressed director of finance but it won't help his patients very much.

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Irreversible pulmonary hypertension after treatment with fenfluramine

SIR,—We wish to reply to the comments made by Drs K Watters and A Le Ridant (26 April, p 1137) regarding our recent case report.[1]

It is obvious that we were describing the natural history of a case of plexogenic pulmonary hypertension. We never attempted to suggest otherwise. In such cases it is essential to look for a specific cause before resorting to the designation "idiopathic." It is therefore not "surprising" that fenfluramine was considered, given that three cases of a possible association with pulmonary hypertension had already been reported.[2,3] Though a chance association was not inconceivable, the appearance of symptoms, signs, and electrocardiographic changes of pulmonary hypertension in two patients after starting treatment with fenfluramine and their regression on withdrawal of the drug seemed significant. This was especially so as these changes recurred in one patient after rechallenge with the drug.

As Drs Watters and Le Ridant acknowledge, our patient's fate was already clear when she presented with exertional dyspnoea four years before her death. Their point that she took no fenfluramine during the last two years of this period is therefore irrelevant, particularly if repeated exposure to this drug can cause progressive, irreversible pulmonary hypertension. It was only the possibility of this association that we wished to raise in our report, and at no point did we attempt to describe this as an "expected side effect" of treatment with fenfluramine.

The writers also stated that we "admitted" our information was "incomplete" and that there was an "absence of comprehensive medical records." We totally refute these serious accusations. The information on this patient was only "incomplete" in that she had not required medical attention in hospital in the period 1977 to 1980 and other detailed information on drug dosage could not be obtained from her general practitioner, despite repeated requests. Records concerning her treatment at this hospital in 1976 and 1984-5, and at the referring hospital, are fully comprehensive.

Drs Watters and Le Ridant admit the need for conscientious drug surveillance. We agree: if such a serious adverse reaction as this has been suggested before it behoves a physician to be vigilant for it and report it. If such a side effect does occur, but only rarely, it will not be commonly reported; this does not mean it does not exist. In an obese cigarette smoker, such as our patient, it would be easy to ascribe breathlessness to another cause and overlook such an association. The difficulties in establishing cause-effect relations are clear, but this case meets the criteria for a "possible" or "conditional" adverse drug reaction report.[4,5] The Committee on Safety of Medicines advises that possible serious or unusual reactions to