Total rise in albumin level (g/l)	Binding coefficient, average $\pm$ SD (true = 0.022) (n = 1000)	Coefficient of variation (%)
3	0.01696 $\pm$ 0.02229	131
6	0.02062 $\pm$ 0.01086	53
9	0.02146 $\pm$ 0.00709	33
12	0.02203 $\pm$ 0.00537	24
15	0.02191 $\pm$ 0.00428	20
18	0.02205 $\pm$ 0.00366	17

coefficients for the three subjects are 0.019, 0.029, and 0.024 respectively. While these show statistically significant differences ($P < 0.05$), they are small enough to be accounted for by the likely differences in albumin:globulin ratio between subjects rather than any genuine differences in albumin binding, for the cuffing method measures binding by all proteins, and globulin cannot be ignored.³

The important question is whether individual determination of a binding coefficient by the proposed method will give a better correction for total protein binding of calcium than would the more straightforward use of average population coefficients for albumin and globulin. The within-subject coefficients of variation for the authors' three subjects average 12%, but a computer simulation of the four-point binding method which incorporates the authors' coefficients of variation for calcium and albumin analyses suggests that even this is likely to be too favourable an estimate. The analysis (see table) shows that the coefficient of variation of the method is dependent on the total rise in albumin achieved by cuffing. With smaller albumin rises not only is the coefficient of variation very high but the binding coefficient tends to be systematically underestimated. There is no support for the authors' assumption that "if more than two timed samples are collected then the likelihood of analytical error causing an erroneous regression line becomes negligible." Their proposed method appears to be unlikely to offer a means for the more accurate correction of calcium values.

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¹ Berry, E M, *et al*, *British Medical Journal*, 1973, **4**, 640.

² Pedersen, K O, *Scandinavian Journal of Clinical and Laboratory Investigation*, 1972, **30**, 321.

³ Hodgkinson, H M, *British Medical Journal*, 1974, **2**, 223.

SIR,—We read with interest the experiences of Dr R W Pain and his colleagues with the tourniquet test as a means of determining protein-bound calcium in plasma (13 December, p 617). They kindly cite our article from 1961 and plan to explore the possibilities of this method. I may be able to save them time by referring them to a later publication,¹ which contains a detailed study of the tourniquet test and the errors involved when using it for the determination of protein-bound calcium by means of in-vivo ultrafiltration.

To my knowledge Niemiro² and Gerbrandy³ were the first to use the tourniquet test for the purpose of determining protein-bound calcium.

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¹ Van Leeuwen, A M, *Acta Medica Scandinavica*, 1964, suppl 422, p 90.

² Niemiro, R, *Bulletin de l'Académie Polonaise des Sciences, Classe II*, 1955, **3**, 167.

³ Gerbrandy, J, *et al*, *Clinical Science*, 1960, **19**, 181.

First-aid treatment of poisoning

SIR,—In considering the emergency treatment of the poisoned child it is perhaps fair to draw a distinction between the management by the full-time health workers listed in your leading article (29 November, p 483) (doctors, nurses, health visitors, and ambulance men) and the part-time first-aiders mentioned by Dr P A B Raffle and his colleagues in their letter (10 January, p 93). The former should have (I do not say do have) a higher standard of training than the part-timers and are more likely to be asked for their advice and help; it is therefore reasonable to expect them to be able to use syrup of ipecacuanha effectively, as the advantages of induced emesis are considerable. I can appreciate, however, that voluntary first-aiders might be consulted so infrequently that it would not be right to train them in its use.

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Natural oestrogen replacement therapy and blood clotting

SIR,—Dr Jean Coope and her colleagues, reporting the results of a double-blind cross-over trial of equine ("natural") oestrogens against placebo in the treatment of 30 patients with menopausal symptoms (18 October, p 139) recorded raised plasma levels of the extrinsic clotting factors VII and X and accelerated prothrombin time after three months' treatment with conjugated equine oestrogens (Premarin 1.25 mg daily). We have recently completed investigations of the effects of both "natural" and synthetic oestrogens on climacteric symptoms, blood biochemistry, and blood clotting in perimenopausal patients.¹ We similarly found a significant increase in the levels of factors X and VII and accelerated prothrombin times in patients who had received either conjugated equine oestrogens (1.25 mg daily) or ethinyloestradiol (0.03 mg daily) for three months.

However, the study of Dr Coope and her colleagues was confined to evaluating equine "natural" oestrogens and their findings imply that other "natural" oestrogens might also accelerate blood clotting factors. Such a conclusion would be at variance with our own data, obtained in a double-blind, between-patient study over six months of the effects of oestrone piperazine sulphate (Harmogen, 3.0 mg daily), ethinyloestradiol (0.03 mg daily), and placebo in 60 perimenopausal patients. At each monthly assessment tests of blood clotting and platelet studies were performed, of which the following are

relevant to the present communication: prothrombin time (BCR)²; platelet aggregation time; fibrinogen assay³; cephalin time; and assays of factors X⁴ and VII.⁵

Of 79 patients admitted, 60 completed the six-month trial: eight of the 19 withdrawn developed adverse effects to the active treatments and 10 patients receiving placebo were withdrawn because of failure to control the severity of menopausal symptoms. The results of coagulation studies are shown in the accompanying table. Significant increases ($P < 0.05$) in the levels of fibrinogen and factors VII and X and acceleration ($P < 0.01$) in prothrombin, cephalin, and platelet aggregation times occurred between the second and sixth months in the ethinyloestradiol group. In the oestrone piperazine sulphate group there were no significant changes in any of these indices at any time during the trial. Follow-up of the 21 patients who continued with oestrone piperazine sulphate for a period of 18 months has not revealed any further change in these indices.

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¹ Aylward, M, *et al*, in preparation.

² Poller, L, Thomson, J M, and Thomas, P W, *British Medical Journal*, 1972, **4**, 391.

³ Aylward, M, Maddock, J, and Parker, R J, *Rheumatology and Rehabilitation*, 1975, **14**, 101.

⁴ Poller, L, Thomson, J M, and Thomas, P W, *British Medical Journal*, 1971, **4**, 648.

⁵ Poller, L, Thomson, J M, and Sear, C H J, *Journal of Clinical Pathology*, 1971, **24**, 626.

Medical writing

SIR,—The large attendance at the teaching seminar on medical writing and editing held on 14 November 1975 under the auspices of the *BMJ* (29 November, p 532) reflects a growing interest in the subject. One hopes that this interest will also be expressed by debate in your columns, and in the columns of other journals, on both the technical and the linguistic aspects of writing papers. May I raise three points now?

First I should like to say a word in defence of the passive voice, the use of which in medical writing is often criticised. The ambiguous "passive of modesty" is, admittedly, indefensible. "Ten patients were investigated by this method" could leave the reader in doubt as to who investigated, the author or another worker, whereas "I investigated 10 patients" or "X investigated 10 patients" is clear. On the other hand the passive, I submit, is better than the active if it enables a sentence, a

Results of coagulation studies (Mean $\pm$ SD) in the three treatment groups at initial assessment and after 6 months

	Oestrone piperazine sulphate (n = 23)		Ethinyloestradiol (n = 20)		Placebo (n = 17)	
	Initial	6 months	Initial	6 months	Initial	6 months
Prothrombin time (s)	12.2 $\pm$ 0.31	12.4 $\pm$ 0.38	12.1 $\pm$ 0.25	11.18 $\pm$ 0.48†	12.2 $\pm$ 0.37	12.2 $\pm$ 0.32
Cephalin time (s)	41.3 $\pm$ 1.6	41.3 $\pm$ 1.5	41.2 $\pm$ 1.8	33.9 $\pm$ 2.5†	41.1 $\pm$ 1.7	41.3 $\pm$ 1.6
Factor VII assay (s)	12.7 $\pm$ 0.18	12.8 $\pm$ 0.19	12.6 $\pm$ 0.29	11.5 $\pm$ 0.31*	12.6 $\pm$ 0.24	12.7 $\pm$ 0.21
Factor X assay (s)	22.8 $\pm$ 0.31	22.7 $\pm$ 0.38	22.6 $\pm$ 0.31	20.4 $\pm$ 0.52*	22.8 $\pm$ 0.40	22.6 $\pm$ 0.31
Plasma fibrinogen (g/l)	2.48 $\pm$ 0.094	2.49 $\pm$ 0.081	2.49 $\pm$ 0.075	2.86 $\pm$ 0.106*	2.42 $\pm$ 0.105	2.46 $\pm$ 0.093
Platelet aggregation time (s)	632 $\pm$ 14.1	630 $\pm$ 18.3	609 $\pm$ 16.2	527 $\pm$ 22.4†	630 $\pm$ 16.0	631 $\pm$ 17.1

Significant changes from initial values: * $P < 0.05$, † $P < 0.01$.
Conversion: SI to traditional units: Fibrinogen 1 g/l = 100 mg/100 ml.

fortiori a paragraph, to open with functional or attention-catching words.

The principle I am defending is the same that applies in choosing the titles of articles. All authorities agree that functional words should occupy the initial or strong position. Thus "Retinoblastoma: a study of the natural history and prognosis in 268 cases" is a better title than "A study of the natural history and prognosis in 268 cases of retinoblastoma"; "Acute myeloid leukaemia treated according to the Hammersmith protocol: a preliminary report" is preferable to "A preliminary report of treatment of acute myeloid leukaemia according to the Hammersmith protocol".

Similarly, "The possible role of nitrosamines in the genesis of oesophageal carcinoma has been suggested by Magee and Barnes and McGlashan *et al*" (12 July, p 61) is a more enticing beginning for a paragraph than "Magee and Barnes and McGlashan *et al* have suggested a possible role of nitrosamines in the genesis of oesophageal carcinoma" would have been. On the other hand, instead of "A recent North American survey has re-examined the problem of chest pain in smokers" (15 November, p 368) I should have preferred "The problem of chest pain in smokers has been re-examined in a recent North American survey". This example also shows one of the pitfalls to which too strict avoidance of the passive can lead. A problem can be examined in a survey, but could a survey, even a computerised one, examine a problem? Examination calls for conscious intellectual effort.

My second point is to recall Sir George Wilson's warning¹ against the misuse of "develop," as in "the patient developed pancreatitis." The patient did not develop pancreatitis; pancreatitis developed in the patient. One develops photographs. An investigator develops disease in experimental animals. But one does not develop disease in oneself—unless one is a self-experimenter, a psychopath, or a cigarette smoker. I expect it was with this third exception in mind that you (13 December, p 607) wrote of smokers "who have already developed chronic bronchitis or coronary artery disease."

Finally, it is disquietening to note in how many otherwise respectable American journals the word "data" is treated as a singular noun. It is true that neuter plural nouns took singular verbs in classical Greek, but I doubt if the perpetrator of "This data was carefully analyzed" was under the influence of deep reading in Plato and Thucydides. He would not have spelled "analysed" with a z.

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¹ Wilson, G, *Monthly Bulletin of the Ministry of Health and the Public Health Laboratory Service*, 1965, 24, 280.

Long-stay mental hospital population

SIR,—The terrible chronicity rate, causing so much suffering to the patients and relatives concerned, reported by Dr Thomas Bewley and Dr Eamonn Fottrell and others (p 675) at Tooting Bec Mental Hospital needs an explanation.

Can a lot of it be due to lack of intensive treatments when the patients were admitted there or elsewhere earlier in their illness? Will these authors also tell us how many now "chronic" schizophrenics and affective states had insulin, electric conversion therapy, the phenothiazines, and finally a modified lower medial leucotomy before being con-

demned to a lifetime of suffering in the chronic wards of Tooting Bec?

When Tooth and Brooke¹ and also Baker² made their calculations on the emptying of mental hospitals, so criticised by Dr Bewley and his colleagues, they had already found, for instance, that over 40% of 10 000 supposedly chronic patients had been able to leave mental hospitals following mostly modified lower medial leucotomies.³ Baker had worked with me, and learnt also at Banstead, what can now be achieved by the use of intensive physical treatments and not "giving up" before *all* such treatments had been used.

Unless we know about the treatment of all these supposedly chronic patients this paper loses most of its value as a guide to whether or not we shall be able to close our mental hospitals and use general hospital units instead.

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¹ Tooth, G C, and Brooke, E M, *Lancet*, 1961, 1, 710.

² Baker, A A, *Lancet*, 1969, 1, 1090.

³ Tooth, G C, and Newton, M P, *Leucotomy in England and Wales 1942-1954*. London, HMSO, 1961.

The third man

SIR,—In his interesting letter about the Everest expedition (10 January, p 92), Dr C R A Clarke mentions the curious sensation of two climbers that their snow-hole bivouac had been shared by a third. Some claim that this is a well-recognised phenomenon in near-exhausted travellers, and it inspired T S Eliot to write in "The Waste Land":

Who is the third who walks always beside you?
When I count, there are only you and I together
But when I look ahead up the white road
There is always another one walking beside you.

In his own notes on the poem Eliot says, "The lines were stimulated by the account of one of the Antarctic expeditions (I forget which, but I think one of Shackleton's): it was related that the party of explorers, at the extremity of their strength, had the constant delusion that there was *one more member* than could actually be counted."

I cannot recall having seen this mentioned in medical literature before. Has it ever been noted and investigated by any psychiatric authority?

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Commercial and NHS factor VIII concentrates

SIR,—One of the inevitable dangers of a journalistic approach to medical problems is that limitations in time (radio or television) or space (newspapers or periodicals) may give rise to a selection of comments made by experts which, when taken out of context and put together for a programme or article, are misleading. This probably arose during the ITN television series "World in action" in which two consecutive programmes attempted to deal with the availability of factor VIII concentrates for haemophilia patients in the United Kingdom.

There is no doubt that the import into the United Kingdom of factor VIII concentrates derived from external sources, however well screened for hepatitis viruses, represents an unequivocal pathway by which

the level of a potentially lethal virus into the whole community is being deliberately increased. Although the absolute magnitude of this problem was exaggerated and over-dramatised by the television programmes, nobody with direct or indirect responsibilities for this phenomenon would wish to belittle the serious nature of the moral and practical dilemmas which face us all.

Perhaps the most important misleading feature of the second television programme was the impression given that the recent and specific injection of £500 000 by the DHSS into the blood transfusion services will have worked its way through by mid-1977, and by that time the necessity to purchase further supplies of factor VIII concentrates will be eliminated. Our own experience indicates that this will not occur, not least because the present NHS production target for factor VIII concentrates is too low. What seems more certain, however, is that by mid-1977 we shall begin to understand that the problems are multifactorial, a good deal more complex than hitherto appreciated, and only partly related to the haemophiliac. In the meantime we would be well advised not to raise the expectations of the patients, their relatives, and the staff of the regional haemophilia centres beyond the certainty that things will improve very slowly, and at the same time look at the problem once again.

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Sodium valproate and platelet function

SIR,—Dr A Richens and Dr S Ahmed (1 November, p 255) and Jeavons and Clark¹ have shown that sodium valproate reduces the frequencies of seizures in epilepsy. The drug is likely to be widely used and, while reported side effects have so far been minor, there has been one report² of a prolonged bleeding time in four out of five patients who also showed coagulation abnormalities. The prolonged bleeding time was attributed to defective platelet function, but one patient was thrombocytopenic. We have therefore studied the effects of sodium valproate on platelet function and coagulation to determine the clinical significance of these findings.

Sodium valproate was added to citrated plasma from six healthy adults to give final concentrations of 0.2, 1.0, and 5.0 g/l corresponding to one, five, and 25 times the therapeutic level. Platelet adhesiveness to glass beads, platelet factor 3 release, and ristocetin- and collagen-induced aggregation were normal. Inhibition of the secondary phase of platelet aggregation following normal primary aggregation with adenosine diphosphate (2.4×10^{-6} mol/l), adrenaline, and thrombin was demonstrated in all six plasmas at 25 times the therapeutic level and, with thrombin, in three plasmas at the therapeutic level. Standard tests of coagulation (prothrombin, partial thromboplastin, thrombin, Reptilase, and Stypven times) were normal at all three concentrations.

Platelet function tests were also performed on 23 patients (aged 4-22 years) taking sodium valproate. Inhibition of the secondary phase of aggregation following primary aggregation with adenosine diphosphate, adrenaline, or thrombin was demonstrated in six patients, five of whom were taking sodium valproate as the sole anticonvulsant.