

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.<sup>3</sup>

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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- <sup>1</sup> Berry, E M, *et al*, *British Medical Journal*, 1973, 4, 640.  
<sup>2</sup> Pedersen, K O, *Scandinavian Journal of Clinical and Laboratory Investigation*, 1972, 30, 321.  
<sup>3</sup> Hodkinson, 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,<sup>1</sup> 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 Niemiro<sup>2</sup> and Gerbrandy<sup>3</sup> were the first to use the tourniquet test for the purpose of determining protein-bound calcium.

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- <sup>1</sup> Van Leeuwen, A M, *Acta Medica Scandinavica*, 1964, suppl 422, p 90.  
<sup>2</sup> Niemiro, R, *Bulletin de l'Académie Polonaise des Sciences, Classe II*, 1955, 3, 167.  
<sup>3</sup> 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.<sup>1</sup> 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

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.

relevant to the present communication: prothrombin time (BCR)<sup>2</sup>; platelet aggregation time; fibrinogen assay<sup>3</sup>; cephalin time; and assays of factors X<sup>4</sup> and VII.<sup>5</sup>

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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- <sup>1</sup> Aylward, M, *et al*, in preparation.  
<sup>2</sup> Poller, L, Thomson, J M, and Thomas, P W, *British Medical Journal*, 1972, 4, 391.  
<sup>3</sup> Aylward, M, Maddock, J, and Parker, R J, *Rheumatology and Rehabilitation*, 1975, 14, 101.  
<sup>4</sup> Poller, L, Thomson, J M, and Thomas, W, *British Medical Journal*, 1971, 4, 648.  
<sup>5</sup> 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