Letters to the Editor

Oral anticoagulation and antithrombin III

We were interested to read the paper by Bull *et al.*¹ attributing the increase in antithrombin III seen in patients on oral anticoagulant therapy to age and underlying disease rather than anticoagulant treatment itself. We have also measured antithrombin III in patients on oral anticoagulant therapy (nicoumalone) but compared results before and after stopping treatment. Two separate series of patients were studied. In both series antithrombin III was measured before stopping and eight days after complete discontinuation, in the first series of seven patients using the method of immunodiffusion with Behringwerke antibody and in the second series of 13 patients using chromogenic substrate assay with chromozym TH.² In the second series seven of these 13 patients were followed up between 3 and 12 months later and repeat assay performed. Both series of patients showed a significant fall in antithrombin III after stopping treatment (see Table) and this change was still present at 3-12 months follow-up. These

findings are in agreement with the findings of Refvem and colleagues³ who also followed antithrombin III activities after stopping anticoagulant treatment. In our study we also performed the ¹²⁵I fibrinogen scan⁴ during the eight-day period after stopping to ensure that changes were not due to rethrombosis during this period. None of the 20 patients studied showed positive scans.

We conclude that oral anticoagulants cause a true rise in antithrombin III activity. Measurements of antithrombin III were also carried out on days 1, 3 and 5 after stopping treatment. The mean fall in antithrombin III activity did not parallel the fall in prothrombin time nor activated partial thromboplastin time; but was maximal on day 8 after discontinuation. This suggests that this change is not an effect on synthesis as the turnover of antithrombin III is about 2-8 days, but on catabolism. We suggest that this increased destruction of antithrombin III is caused by increasing in vivo thrombin generation as the normal form of prothrombin is resynthesised when oral anticoagulants

are discontinued.

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References

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- 2 Abildgaard U, Lie M, Odegard OR. Antithrombin (heparin cofactor) assay with "new" chromogenic substrates (S2238 and Chromozym TH). *Thromb Res* 1977;11:549-53.
- 3 Refvem O, Faberhol MK, Abildgaard U. Changes in antithrombin III levels following cessation of anticoagulant therapy. *Acta Med Scand* 1973;193:307-9.
- 4 Kakkar VV, Nicolaides AN, Renney JTG, *et al.* ¹²⁵I-labelled fibrinogen test. *Lancet* 1970;ii:540-2.

Antithrombin III activities before and after stopping oral anticoagulants

Antithrombin III antigen (%)			
First series of patients	†Before	†8 days after stopping	
1	91	90	
2	112	100	
3	102	81	
4	93	87	
5	98	87	
6	101	100	
7	105	100	
Mean	100.3	92.1	

Antithrombin III activity (%)			
Second series of patients	*Before†	*8 days after stopping	†3-12 months after stopping
1	94	86.5	88
2	92	84	NT
3	102	102.5	102.5
4	88	79	83
5	86	83	NT
6	94.5	87	NT
7	94.5	96	87
8	97	87	88
9	102	96	99
10	102.5	100	86
Mean	95.3	90.1	90.5

*p < 0.005 using paired t test.

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Accidental transplantation of tumour cells

In the February issue of your journal, Forbes *et al.*¹ reported that "patients dying of malignant disease confined to the brain are the only cancer subjects who should be considered as sources of organs for transplantation."

We disagree with this opinion, as, from our own experience we find that it is extremely difficult to be absolutely certain that the tumour is confined to the brain, even after a very thorough necropsy of the donor. Although, it is still a widely accepted fact that visceral metastasis of central nervous system (CNS) tumours are an exception.² Nevertheless, our own research^{3,4} has clearly demonstrated that all primary CNS tumours, regardless of their histological type, can cause extraneural metastasis. In 1977, we studied 248 observations of extraneural metastasis found in the world literature, which for the most part occurred from glioblastomas and astrocytomas. These studies consisted mainly of subjects who had undergone several craniotomies, but spontaneous metastases, which are sometimes the first