

The psychological consequences of diets that restrict energy intake are disputed. Our observations suggest that irritability and waking early in the morning were common in the third week of the diet. Whether these behavioural changes were related to decreased plasma concentrations of tryptophan could be investigated by supplementing the diet with tryptophan. There would be considerable interest if supplementation improved the compliance with, and effectiveness of, dieting. Unfortunately, pharmaceutical preparations of tryptophan have been withdrawn because of their suspected association with the eosinophilia-myalgia syndrome.<sup>5</sup> It may be feasible, however, to investigate the effect of supplementation with tryptophan by manipulating the dietary intake of tryptophan and other

amino acids. Tryptophan remains important to the understanding of the relation between food intake and brain function.

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## Impaired fibrinolytic capacity and early recurrent spontaneous abortion

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Impaired fibrinolytic activity in blood has been claimed to contribute to the development of deep venous thrombosis.<sup>1</sup> Placental infarction is often found in abortions associated with lupus-like anticoagulants.<sup>2</sup> We report the fibrinolytic capacity in the plasma of women suffering from recurrent spontaneous abortions.

### Patients, methods, and results

We studied 20 women aged 22-41 (mean 34) years with at least three episodes of spontaneous abortion occurring before the eighth week after the last menstrual period. Results of hystero-graphy and hormonal evaluation were normal in all cases. Each couple was assessed to have normal karyotypes. Women were negative for antispermatozoa, antinuclear, and anti-deoxyribonucleic acid antibodies and had developed antibodies to their partner's human leucocyte antigens. The absence of lupus-like anticoagulant was assessed by normal values of kaolin clotting time, activated partial thromboplastin time, tissue thromboplastin inhibition, and platelet neutralisation. Results of an enzyme linked immunosorbent assay (ELISA) for antiphospholipid and anticardiolipin antibodies were negative.

Fibrinolytic capacity was studied by using a 10 minute venous occlusion test between 9 and 11 am in non-pregnant women at least three months after the last abortion. A control group of 32 apparently healthy women aged 20-39 (mean 32) years was studied

simultaneously. Plasma euglobulin fibrinolytic activity was measured by the euglobulin clot lysis time, tissue type plasminogen activator related antigen by an ELISA, plasminogen activator inhibitor activity by the method of Eriksson *et al.*<sup>3</sup> Postocclusion plasminogen activator values were corrected for the change in packed cell volume by using the correction factor (100 poststasis packed cell volume)/(100 prestasis packed cell volume). Variations in variables induced by venous stasis were assessed by using the "delta %" ( $\delta$  %) criterion, defined as (poststasis assay value - prestasis assay value)/prestasis assay value.

The table shows that patients had significantly less shortening of the euglobulin clot lysis time and a smaller increase in tissue type plasminogen activator activity after venous stasis, and significantly higher plasminogen activator inhibitor activity before venous stasis.

### Comment

Hypofibrinolysis generally stems from either deficient release of tissue type plasminogen activator or raised plasma concentrations of plasminogen activator inhibitor masking the fibrinolytic response to venous occlusion.<sup>1</sup> We found evidence of these abnormalities in 13 of the 20 women investigated for recurrent abortions. Deficient activator release (eight patients) was not corrected by desmopressin infusion (0.4  $\mu$ g/kg).

The relevance of these data is unclear. Hypofibrinolysis is frequently associated with thrombosis.<sup>1</sup> Abortions occurred very early and pathological examination of the placenta could not be performed. Fibrinolysis is also involved in the enzymatic basis of trophoblast invasiveness.<sup>4</sup> Hypofibrinolysis in mothers might be acquired and might explain a defect of plasminogen activation in trophoblast cells. The reason behind this remains to be clarified.

Impaired fibrinolytic capacity seems to be a common feature in women with early recurrent spontaneous abortions of unknown origin.

Mean (SD) [range] euglobulin clot lysis time and immunoassayable tissue type plasminogen activator variations after venous occlusion (delta %), and values of plasminogen activator inhibitor activity before venous occlusion in the control group and in 20 women with early spontaneous recurrent abortion

|          | Euglobulin clot lysis time<br>( $\delta$ %) | Tissue plasminogen activator<br>( $\delta$ %) | Plasminogen activator<br>inhibitor activity<br>(U/ml) |
|----------|---|---|---|
| Controls | -47 (8) [-70 to -30]                        | +85 (22) [+40 to +135]                        | 5.5 (5.0) [0 to 16.5]                                 |
| Patients | -25 (28) [-73 to 0]                         | +62 (49) [0 to +169]                          | 10.6 (8.3) [3 to 28.2]                                |
| p Value* | <0.01                                       | <0.02   | <0.01   |

\*U test.

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