

aeroplanes is 75 kPa, so that the arterial oxygen pressure in normal people is about 7.3 kPa. The condition of patients who already have hypoxia may deteriorate further during a flight if they are not given added oxygen.

For these reasons patients with high spinal injuries are at risk during journeys by aeroplane. We make the following recommendations for such patients:

(1) Lung function should be adequate and stable before transfer.

(2) Humidification of inspired air should be adequate before and during transport, particularly for patients with an endotracheal tube or tracheostomy. If secretions are sticky 2 ml of warm saline can be passed down the endotracheal tube or tracheostomy tube at frequent intervals.

(3) Supplemental oxygen should be available.

(4) Patients should be accompanied by someone trained in manoeuvres to clear secretions from patients with spinal injuries<sup>4</sup> and prepared to perform tracheal suction frequently.

(5) Intravenous atropine should be available.

Tracheal suction in patients with high spinal injuries may precipitate life threatening bradycardia.<sup>5</sup> The incidence of such bradycardia is reduced by preoxygenation before suction and the skilful use of the suction catheter. If appreciable bradycardia develops intravenous atropine should be given. Patients prone to serious bradycardias may be treated with an oral adrenal agonist such as orciprenaline before the flight.

We believe that if these recommendations are adopted patients with high spinal injury may be transported by air more safely.

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## Plasma concentrations of tryptophan and dieting

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Mean (SD) concentrations of energy metabolites and amino acids before and during diet

|                                     | Men         |             | Women       |             |
|-------------------------------------|-------------|-------------|-------------|-------------|
|                                     | Before      | During      | Before      | During      |
| Glucose (mmol/l)                    | 4.4 (0.6)   | 3.9 (0.6)   | 3.7 (0.8)   | 3.7 (0.2)   |
| Lactate (mmol/l)                    | 1.91 (0.44) | 1.61 (0.22) | 1.64 (0.15) | 1.68 (0.30) |
| Butyrate (mmol/l)                   | 0.33 (0.28) | 0.35 (0.19) | 0.33 (0.20) | 0.41 (0.39) |
| Free fatty acids (mmol/l)           | 1.01 (0.70) | 0.76 (0.47) | 0.92 (0.47) | 0.96 (0.30) |
| Branched chain amino acids (μmol/l) | 405 (61.7)  | 455 (65.9)  | 344 (65.7)  | 336 (51.6)  |
| Alanine (μmol/l)                    | 339 (53.6)  | 245 (48.6)† | 261 (59.0)  | 270 (50.7)  |
| Glutamine (μmol/l)                  | 373 (57.7)  | 356 (65.1)  | 373 (58.8)  | 384 (44.9)  |
| Tryptophan (μmol/l)                 | 57.5 (12.0) | 45.2 (6.4)† | 49.8 (11.8) | 40.6 (4.8)* |

\*p<0.05. †p<0.02.

Dieting to lose weight is commonplace in Western societies. Numerous popular publications advise on how diets can be made easy, effective, and healthy. They often speculate on the relation between food intake and subjective experience, but this has generated only one important scientific hypothesis in the past 20 years.<sup>1</sup> None of the brain enzymes that convert plasma tryptophan to serotonin approaches saturation with substrate. A fall in the plasma concentration of tryptophan should therefore reduce the rate of synthesis and hence the serotonin concentration. Serotonin is believed to be important in regulating appetite, sexual activity, and the control of impulses, and strong circumstantial evidence links abnormalities in serotonin concentration with depression. Indeed, total exclusion of tryptophan from the diet produces depression.<sup>2</sup> No systematic study has been made of changes in the plasma concentrations of key amino acids in mildly overweight subjects taking low energy diets to lose weight.

### Subjects, methods, and results

Eight men and eight women with a body mass index within the normal range for Western societies (men 21-30 kg/m<sup>2</sup>; women 21-27 kg/m<sup>2</sup>) were recruited to take a weight reducing diet of 4.18-5.02 MJ/day. The

study was approved by the local ethics committee. Blood samples were taken after an overnight fast before the diet and during the third week of dieting. The women were studied in the middle of consecutive menstrual cycles and started dieting with the onset of the menses.

The diet was designed by the department of nutrition and dietetics, Oxford University. The subjects were given information about high and low energy foods and recommended a daily dietary allowance of 0.5 l skimmed milk; 20 g polyunsaturated margarine; two servings of lean meat (60 g), white fish (120 g), cheese (30 g), cottage cheese (90 g), one egg, or one small carton of yoghurt; five slices of wholemeal bread; one serving of wholegrain breakfast cereal; and two portions of fruit.

Blood was collected in heparinised tubes and the plasma separated by centrifugation at 2000 rpm and stored at -30°C. Assays of metabolites are described elsewhere.<sup>3,4</sup> Results were compared with the paired *t* test (two tailed).

All the subjects lost weight; the men lost a mean of 5.4 kg (95% confidence interval 4.7 to 6.1 kg) and the women 2.9 kg (2.3 to 3.6 kg). Food diaries showed good compliance with dietary recommendations. Dieting had no effect on the plasma concentrations of glucose, lactate, 3-hydroxybutyrate, branched chain amino acids, glutamine, or free fatty acids (table). While dieting the men had decreased plasma concentrations of alanine and both the men and the women had lower tryptophan concentrations. The ratio of the mean plasma concentrations of tryptophan to branched chain amino acids was also reduced (0.15 (SD 0.04) before v 0.11 (0.02) during the diet; p<0.02).

### Comment

The weight reducing diet decreased the plasma concentrations of tryptophan in both the men and the women. The effect was greater in the men, but this may be explained by their greater reduction in energy intake to achieve 5.02 MJ/day. The diet aimed at decreasing carbohydrate and fat intakes; protein intake was maintained and provided 800-1200 mg tryptophan each day, which is considerably greater than either the minimum recommended amount (250 mg) or the "safe" amount (500 mg). Conventional dieting is thus likely to reduce tryptophan concentrations and hence the rate of synthesis of serotonin in the brain.

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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