

difference between the mode of delivery or the age of the babies at scanning and the incidence of ventricular asymmetry. Asymmetry of brain has been found in all age groups from the fetus to the adult.<sup>4-6</sup> We believe that asymmetry of the lateral ventricles and probably that of the brain is influenced by genetic factors or environmental events that occur during the growth of the brain and not by the pressure effect through the birth canal.

In summary, we report four types of ventricular asymmetry based on the sonographic findings of 1000 normal Chinese neonates. Although our figures do not reflect the true ventricular contours, these findings may have some value for future studies of the neonatal brain.

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## Plasma vitamin K<sub>1</sub> concentrations in cystic fibrosis

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**SUMMARY** Plasma concentrations of vitamin K<sub>1</sub> were similar in 37 patients with cystic fibrosis (median 46 ng/l) and 16 controls (49 ng/l). The plasma concentrations were lower than those previously described in adults, but higher than in neonates. There was no association between an increase in prothrombin time and vitamin K<sub>1</sub> plasma concentration.

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Children with cystic fibrosis suffer from malabsorption and are, therefore, prone to deficiencies of fat soluble vitamins. Clinical problems secondary to vitamin K deficiency, however, are rare in cystic fibrosis.<sup>1</sup> Komp and Selden reviewed 59 patients and found only four with an increased prothrombin time and possible vitamin K deficiency.<sup>2</sup> A subsequent study, however, measuring factor II antigen and activity suggested that vitamin K<sub>1</sub> deficiency is common in cystic fibrosis.<sup>3</sup>

The measurement of vitamin K<sub>1</sub> is technically difficult and there are no data on plasma concentrations in children. We therefore decided to measure plasma concentrations of vitamin K<sub>1</sub> in children with cystic fibrosis and also a group of control children.

#### Patients and methods

Blood samples (5 ml) were collected from 37 patients (28 fasting) with cystic fibrosis (mean age 10.6 years, range 2-23 years) and 16 children (controls, all non-fasting) who were having venipunctures at the general outpatients' clinic (mean age 7.6 years, range 3-14 years). The children with cystic fibrosis were attending the Regional Centre at St James's University Hospital where routine annual assessment included the measurement of plasma concentrations of vitamins A and E, faecal fats, liver function tests, and prothrombin time. Plasma concentrations of vitamin K<sub>1</sub> were measured by high performance liquid chromatography coupled to dual cell electrochemical detection.<sup>4</sup> The limit of sensitivity for the assay was 4 ng/l. Statistical analysis was by Spearman's rank correlation and the Mann-Whitney U Test.

Ethical approval was obtained from the local ethics committee.

#### Results

The individual plasma concentrations of vitamin K<sub>1</sub> are shown in the figure. Nine children (two controls)

had plasma vitamin K<sub>1</sub> concentrations below the limit of detection (4 ng/l). There was no difference in the plasma vitamin K<sub>1</sub> concentrations in the non-fasting (mean 71.1, median 45 ng/l) and fasting (mean 76.6, median 48 ng/l) patients with cystic fibrosis. Therefore, the two groups were amalgamated and the results compared with the controls. One of the children in the control group had a very high plasma concentration of vitamin K<sub>1</sub> (2115 ng/l) and was excluded when determining the mean. Although the mean plasma concentration of vitamin K<sub>1</sub> was lower in the patients with cystic fibrosis (75.2 ng/l) than in the controls (172.5 ng/l), the median values were similar (46 and 49 ng/l respectively).

Nine patients had a prothrombin time index of 1.2 or greater and their plasma concentrations of vitamin K<sub>1</sub> are shown in the figure. There was no association between a raised prothrombin time index and plasma concentrations of vitamin K<sub>1</sub> (Mann-Whitney U test,  $p > 0.2$ ).

There was no correlation between the plasma

concentration of vitamin K<sub>1</sub> and age, faecal fats, plasma concentrations of vitamins A and E, or the clinical state of the patient (Shwachman and Crispin-Norman scores) (Spearman's rank correlation,  $p > 0.1$ ).

### Discussion

There was considerable interindividual variation in the plasma concentrations of vitamin K<sub>1</sub>. There have been no previous studies of plasma concentrations of vitamin K<sub>1</sub> in children outside the neonatal period. The concentrations detected in the control children were lower than that described in healthy adults (mean 260 ng/l, median 210 ng/l, range 100–660 ng/l)<sup>5</sup> and higher than that reported in newborn babies (mean 18 ng/l, median 16 ng/l, range 4–45 ng/l).<sup>6</sup>

Although the mean plasma vitamin K<sub>1</sub> concentration in patients was lower than that in controls, the median values were similar. Case reports of undiagnosed patients with cystic fibrosis presenting with bleeding problems describe individuals under the age of six months.<sup>1</sup> Our results suggest that children with cystic fibrosis of the age range studied (no infants) do not have vitamin K<sub>1</sub> deficiency.

The relationship between plasma and hepatic concentrations of vitamin K<sub>1</sub> is unknown. Neonatal hepatic concentrations of vitamin K<sub>1</sub> are significantly lower than in adults. Vitamin K<sub>1</sub> is responsible for the  $\gamma$  carboxylation of clotting factors II, VII, IX, and X and the minimum plasma concentration required for adequate  $\gamma$  carboxylation is unknown. The prothrombin time appears to be an inadequate marker of vitamin K<sub>1</sub> state. There was no association between prothrombin time and plasma concentration of vitamin K<sub>1</sub>. The patients with an increase in prothrombin time were slightly older (mean age 12.9 years) than the group in general and it is probable that other factors are involved in causing an increase in prothrombin time.

Routine vitamin K<sub>1</sub> supplementation for patients with cystic fibrosis is not required. Further studies are required to see whether oral supplementation has any effect on those patients with an increase in prothrombin time.

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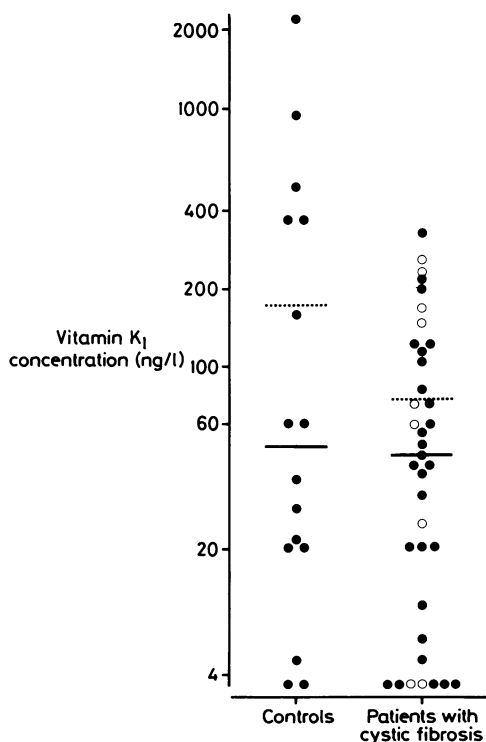


Figure Plasma concentrations of vitamin K<sub>1</sub> in controls and patients with cystic fibrosis. Patients with prothrombin time index  $> 1.2$  are indicated by open circles. The mean (----) and median (—) values are shown.

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## Water intoxication and hyponatraemic convulsions in neonates

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**SUMMARY** We studied two neonates fed diluted formula and excessive water who developed hyponatraemic convulsions; treatment included intravenous hypertonic saline and water restriction. Educating mothers is important to stop recurrences.

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From 1967 to 1983 there were 24 cases of infants with water intoxication reported in the literature; their ages ranged from 3 weeks to 11 months.<sup>1-4</sup> We report two neonates with seizures secondary to water intoxication.

### Case reports

#### CASE 1

A 20 day old girl, the product of a full term, normal delivery, was the first child born to a healthy 20 year old mother. The baby had been well since birth. On the day of admission she was taken to hospital because of irritability and slight abdominal distension not associated with vomiting or diarrhoea. The physical examination was unremarkable and after reassuring the mother the child was sent home. One hour later the baby had a tonic-clonic convulsion and was readmitted to hospital where she was treated with intravenous diazepam. Blood was taken for biochemical and microbiological investigations. The child was given 5% dextrose in one fifth normal saline intravenously.

Physical examination on admission (after intravenous diazepam) showed an unconscious child with a rectal temperature of 36.5°C, pulse rate 120/minute, and respiratory rate 36/minute; there was no anaemia, jaundice, or oedema. The anterior fontanelle was open and soft, the abdomen was slightly distended with normal bowel sounds, and

there was no hepatosplenomegaly. The patient responded to deep pain by moving her extremities; her pupils were equal and reactive to light.

The white cell count was  $5.37 \times 10^9/l$  with 60% polymorphonuclear cells and 40% lymphocytes, and the haemoglobin concentration was 107 g/l. A microscopic examination of the urine was normal with a specific gravity of 1.005. The blood urea nitrogen was 3.2 mmol/l and the blood glucose concentration 7.8 mmol/l. The concentration of sodium in the serum was 117 mmol/l, potassium 4.8 mmol/l, chloride 92 mmol/l, and carbon dioxide 15 mmol/l. The osmolality of the serum was 240 mmol/kg and of the urine 83 mmol/kg. The cerebrospinal fluid was normal; culture of blood, urine, and cerebrospinal fluid gave negative results.

Because of the severe hyponatraemia in an otherwise healthy infant a detailed history of feeding was taken from the mother. On the day before admission the baby had been given 2 oz of diluted formula consisting of one tablespoon of S26 powdered milk (Wyeth (Ireland) Ltd) in 3 oz of water every four hours; in between each feed the mother gave the infant 4 oz of water. Throughout this period she passed a large quantity of urine. The diagnosis of hyponatraemia caused by excess feeding of water was made and the baby was managed by restricting fluid intake. No further convulsion occurred and the serum electrolytes became normal on the following day.

#### CASE 2

An 8 day old boy, the fifth child of an impoverished family, was born at term after a normal vaginal delivery, weighing 3020 g. The Apgar scores were 9 and 10 at one and five minutes, respectively. The baby had no problem during his nursery stay. At home he was fed 2 oz of a normal dilution of S26