

EFFECTS OF ACUTE DEHYDRATION ON COMPUTERISED TOMOGRAPHIC ASSESSMENT OF CEREBRAL DENSITY AND VENTRICULAR VOLUME

SIR,—Computerised tomography (CT) has revealed cerebral abnormalities in clinical conditions such as schizophrenia¹ and alcoholism.² The cause of these abnormalities, which include enlarged ventricles, is not known, although an atrophic process has been suggested. However, certain CT abnormalities are reversible, and nutrition, hydration, and medication have been considered as possible factors.^{3,4} Furthermore, post-mortem studies have not always shown exact correlation with scans done during life.⁵ It is thus possible that some CT changes seen in clinical conditions might be artifacts. In particular, increases in ventricular size could be related to the state of hydration.

In a preliminary investigation into the effects of dehydration, one of us (A. R. M.) was scanned on a CT 10/10 scanner. A second scan, 2 days later, was done after total fluid restriction for 24 h and an oral dose of 40 mg frusemide. Both scans were done at the same time of day. Measurements immediately before each scan showed a change in plasma osmolality from 280 to 290 mosmol/l and a resting pulse increase from 70 to 100/min. Also, a moderate headache was experienced after dehydration. Floppy discs were reviewed on the scanner's video display unit and analysed with the E.M.I. diagnostic enhancement package.

Pixels with densities of 0–15, 0–20, and 0–25 Hounsfield units (HU) were selected to be incorporated as ventricle, and then all slices which showed lateral ventricle were measured to obtain the total volume of the lateral ventricle. This included the anterior horns, body, and trigone; the posterior horns were not visualised and the temporal horns were so small that they could not be measured. The ventricular brain ratio (VBR) was determined by taking the largest ventricular area divided by brain area $\times 100$. Brain density was measured with a circular "region of interest" marker selecting pixels between 20 and 70 HU. Consistency between scans was assessed with an E.M.I. phantom and total pixel numbers between 20 and 70 HU in the scans used were measured and shown to have less than a 1% variation. The results are shown in tables I and II.

TABLE I—TOTAL VENTRICULAR VOLUME AND VBR

Scan	0–15 HU		0–20 HU		0–25 HU	
	Vol. (ml)	VBR	Vol. (ml)	VBR	Vol. (ml)	VBR
Predehydration	1.65	0.43	4.77	1.09	14.29	3.20
Postdehydration	0.79	0.32	2.56	0.86	6.73	2.00

TABLE II—MEAN BRAIN DENSITY FOR PIXELS BETWEEN 20 AND 70 HU

	L. frontal area (HU)	L. thalamus (HU)	L. occipital area (HU)
Predehydration	34.459	37.081	36.5149
Postdehydration	39.189	39.189	40.2709

It is impossible to draw firm conclusions from scans of one individual. Variation in results may be due to errors produced in positioning, despite the apparent comparability of CT slices. There may also be variation in the proportion of grey to white matter included when measuring density. However, despite these precautions, this preliminary study demonstrates a decrease in ventricular size and an increase in brain density with acute dehydration. This does not support the hypothesis that observed

increases in cerebral ventricular size on CT scan might be artifactually produced by dehydration in the patients studied.

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NORTHERN FOWL MITE (ORNITHONYSSUS SYLVIARUM) IN OCCUPATIONAL ASTHMA OF POULTRY WORKERS

SIR,—Many workers with intense and prolonged exposure to organic inhalant antigens have occupational respiratory diseases the aetiology of which may include hypersensitivity; one such group is poultry workers. A *Lancet* editorial¹ has emphasised the occupational hazards facing animal workers and noted the danger of animal-related allergies. Inhalation of mite-laden dust frequently results in allergic respiratory disease, and grain storage mites can cause work-related asthma and rhinitis in farmers.² The northern fowl mite (*Ornithonyssus sylviarum*), found in all temperate and north temperate regions and in some subtropical areas as well, is a vicious bloodsucker which has been called the most important external parasite of poultry.³ Our interest in occupational asthma led us to investigate the possible role of this mite in allergic respiratory illness in poultry workers.

We studied 16 poultry farmers with a clinical history of allergic rhinitis, 13 of whom also had bronchial asthma. When at work in the poultry house all of them reported respiratory illness; however, outside this environment most of them noted a marked reduction in symptoms. Controls included 27 atopics with similar respiratory problems but not exposed occupationally to poultry and 29 non-atopics (12 with and 17 without occupational exposure to poultry).

Prick test results are shown in the table.

POSITIVE PRICK SKIN TESTS WITH SIX POULTRY ANTIGENS

Poultry exposure	No.	No. positive to:					
		NFM	Poultry feed	Poultry litter	Chicken serum	Turkey serum	Mixed feathers
Atopic:							
Yes	16	10	5	4	3	2	3
No	27	2	0	1	0	1	0
Non-atopic:							
Yes	12	0	0	0	0	0	0
No	17	0	0	0	0	0	1

NFM = northern fowl mite.

Positive skin test results were seen in 14 of 16 atopic poultry workers but in only 4 of 27 non-poultry-exposed atopics ($p < 0.00004$). The numbers with NFM antigen positive skin tests were 10 and 2, respectively ($p < 0.0002$). 3 atopic poultry workers, who were skin test positive for the common house dust mite *Dermatophagoides farinae*, were skin test negative for NFM, and 3 atopic poultry workers with positive skin tests for NFM were negative to *D. farinae*, indicating incomplete cross-antigenicity.

Using NFM antigen bound discs prepared in our laboratory, we determined specific IgE antibody levels for NFM by radioallergen sorbent test (RAST). Positive RAST scores (2 or greater) were found for more than 60% of the atopic poultry workers with positive skin tests for NFM.

Using a stationary personal sampler we collected total poultry workplace dust samples on 37 mm Nucleopore membrane filters. Scanning electron microscopy of selected samples confirmed the presence of mites and mite parts in poultry house dust.

1. Editorial. Occupational hazards for animal workers. *Lancet* 1981; ii: 789–90.

2. Cuthbert OD, Brostoff J, Wraith DG, Brighton WD. Barn allergy. Asthma and rhinitis due to storage mites. *Clin Allergy* 1979; 9: 229–36.

3. De Vaney JA. A survey of poultry ectoparasite problems and their research in the United States. *Poultry Sci* 1978; 57: 1217–20.

1. Reveley AM, Reveley MA, Clifford CA, Murray RM. Cerebral ventricular size in twins discordant for schizophrenia. *Lancet* 1982; i: 540–41.

2. Ron MA, Acker W, Lishman WA. Computerised axial tomography in alcoholics. *Acta Psychiatr Scand* 1980; suppl 286, 62: 41–46.

3. Beniston J, Reza M, Winter J, Wilson G. Steroids and apparent atrophy on CT scans. *J Comp Assist Tomog* 1978; 2: 16–28.

4. Heinz ER, Martinez J, Haenggeli A. Reversibility of cerebral atrophy in anorexia nervosa and Cushing's syndrome. *J Comp Assist Tomog* 1977; 1: 415–18.

5. Sarwar M, McCormick WF. Decrease in ventricular and sulcal size after death. *Radiology* 1978; 127: 410–11.

To establish whether inhalation of NFM allergen could elicit an asthmatic reaction we did a provocation test in a 30-year-old poultry farmer. He had a history of wheezing and shortness of breath associated with poultry work, and had a positive skin test (4+) and positive RAST to NFM. Bronchial challenge with NFM produced a transient fall of 25% in his FEV₁ and a 62% reduction in forced expiratory flow volume at 25% of vital capacity.

The presence of NFM in the poultry houses together with the clinical histories, positive skin tests and specific IgE assays, and positive bronchial provocation, establish *O. sylvaticum* as a cause of allergic respiratory disease in poultry workers. We conclude that sustained exposure to the northern fowl mite may lead to significant workplace hypersensitivity and that this exposure may well be an occupational health hazard of poultry farming.

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PRENATAL DIAGNOSIS OF HOMOCYSTINURIA

SIR,—Prenatal diagnosis of the more common form of homocystinuria, caused by deficiency of cystathionine- β -synthase, is theoretically feasible since cystathionine- β -synthase activity can be demonstrated in cells cultured from mid-trimester amniotic fluid.^{1,2} To our knowledge no fetus with deficiency of this enzyme has yet been described, although a normal fetus has been detected in some "at risk" pregnancies.^{2,3} We describe here our experience of 1 prenatal diagnosis in two pregnancies in a family at risk for cystathionine- β -synthase deficiency homocystinuria.

In this Norwegian family two sisters, born to unrelated parents, were found to have the severe form of the disease. The first child, born in 1970, showed retarded development by 2 years of age and subsequently acquired a "Marfan"-like appearance, pectus carinatum, ectopia lentis, fair brittle hair, and a high arched palate. Investigations revealed homocystinaemia (117 μ mol/l; normal, absent), methioninaemia (685 μ mol/l; normal, 18–26) and low plasma cystine, which were only partly improved by prolonged treatment with pyridoxine 360 mg daily. The second child, born in 1972, had similar clinical and biochemical features. The enzymic defect was confirmed in cultured skin fibroblasts of both patients (table 1).

Two subsequent pregnancies have been monitored for homocystinuria by amniocentesis at 16 weeks' gestation. Cystathionine- β -synthase was assayed in sonicates of cultured amniotic fluid cells, in the presence and absence of added pyridoxal-5'-phosphate (co-factor for the enzyme). A radioisotopic assay was used as previously described,⁴ except that paper chromatograms were developed for at least 60 h to ensure adequate separation of ¹⁴C-cystathionine from another radioactive compound formed in the assay.

In the first of these pregnancies, cystathionine- β -synthase activity was normal in cultured amniotic fluid cells, indicating an unaffected fetus. After the birth of the child, the genotype was confirmed by the absence of homocystine in urine and by detection of normal enzyme activity in cultured skin fibroblasts. This child is now 3 years of age and has progressed normally.

In the second pregnancy, the finding of much reduced enzyme activity in cultured amniotic fluid cells indicated an affected fetus. The stimulation of residual cystathionine- β -synthase activity by added pyridoxal-5'-phosphate, in contrast to the much lower stimulation of control enzyme, provided further evidence of a

TABLE 1—CYSTATHIONINE β -SYNTHASE ACTIVITY IN CULTURED CELLS

	Cystathionine- β -synthase activity (nmol/h/mg)	
	No added PP	1 mmol/l PP
<i>Cultured skin fibroblasts:</i>		
Control range (n=8)	3.6–25.7	4.9–32.1
Patient 1	ND	ND
Patient 2	0.05	0.07
Sibling (1st pregnancy)	4.3	7.4
<i>Cultured amniotic fluid cells:</i>		
Control range (n=12)	4.4–40.6	5.7–47.7
1st pregnancy	13.5	15.4
2nd pregnancy	0.038	0.18
<i>Cultured Fetal Fibroblasts:</i>		
Control range (n=5)	14.5–48.3	16.2–57.1
Affected fetus (2nd pregnancy)	0.08	0.3

PP = pyridoxal-5'-phosphate. ND = none detected.

TABLE 2—CONVERSION OF ¹⁴S-HOMOCYSTINE TO CYSTEINE AND METHIONINE IN CULTURED CELL MONOLAYERS

	¹⁴ S sulphur aminoacid formed (nmol/mg)	
	Cysteine	Methionine
<i>Cultured amniotic fluid cells:</i>		
Control	3.0	6.1
2nd pregnancy	0.07	5.2
<i>Cultured skin fibroblasts:</i>		
Control range (n=10)	0.54–6.3	4.5–14.1
Homocystinuria* range (n=11)	0.023–0.17	5.1–9.6

*Cystathionine- β -synthase deficiency.

mutant enzyme in these cells. The diagnosis was confirmed by analysis of the conversion of ¹⁴S-homocystine to cysteine and methionine in amniotic fluid cell monolayer culture⁵ (table 2). Much reduced formation of ¹⁴S-cysteine, with formation of normal quantities of ¹⁴S-methionine, provides further evidence of deficient cystathionine- β -synthase activity in these cells. The parents decided to terminate the pregnancy and the enzyme deficiency was confirmed in the aborted fetus by assay of cultured fetal fibroblasts (table 1).

Our experience indicates that homocystinuria due to cystathionine- β -synthase deficiency can be added to the list of inherited metabolic diseases which can be reliably diagnosed in utero.

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PRENATAL ECHOCARDIOGRAPHIC SCREENING FOR EBSTEIN'S ANOMALY FOR MOTHERS ON LITHIUM THERAPY

SIR,—An association between Ebstein's anomaly of the tricuspid valve and maternal therapy with lithium has been reported,¹ and, in a register of "lithium babies" Weinstein and Goldfield² collected 143 babies, in whom the incidence of congenital heart disease was 7.6% (normal 0.88%) and of Ebstein's anomaly 2.8% (normal only 1 in 20 000 total births³).

5. Fowler B. Transsulphuration and methylation of homocysteine in control and mutant human fibroblasts. *Biochim Biophys Acta* (in press).

1. Nora JJ, Nora AH, Toews WH. Lithium, Ebstein's anomaly, and other congenital heart defects. *Lancet* 1974; ii: 594–95.

2. Weinstein MR, Goldfield MD. Cardiovascular malformations with lithium use during pregnancy. *Am J Psychiatry* 1975; 132: 529–31.

3. Hoffman JIE, Christianson R. Congenital heart disease in a cohort of 19, 502 births with long term follow-up. *Am J Cardiol* 1978; 42: 641–47.

1. Uhlenhuth RW, Mudd SH. Cystathionine synthase in tissue culture derived from human skin. Enzyme defect in homocystinuria. *Science* 1968; 160: 1007–09.

2. Birtles AH, Carson NA. Tissue culture techniques as an aid to prenatal diagnosis and genetic counselling in homocystinuria. *J Med Genet* 1973; 10: 120–21.

3. Fleisher LD, Longhi RC, Tallan HH, Beratis NG, Hirschhorn K, Gauld GE. Homocystinuria: Investigations of cystathionine synthase in cultured fetal cells and the prenatal determination of genetic status. *Pediatrics* 1974; 85: 677–80.

4. Fowler B, Kraus J, Packman S, Rosenberg LE. Homocystinuria: Evidence for three distinct classes of cystathionine β -synthase mutants in cultured fibroblasts. *J Clin Invest* 1978; 61: 645–53.