CENTRAL NERVOUS SYSTEM LEUKAEMIA

SIR,—We read with interest the article by Dr Nesbit and others (June 27, p. 1386) on isolated central nervous system acute lymphocytic leukaemia in children. In this very helpful article Nesbit et al. state that "CNS relapse rates are lower in patients receiving effective treatment before CNS symptoms arise, but the bone marrow relapse rate was not significantly affected by prophylactic therapy". However, we do not find data to support their later contention that "the improved survival of childhood ALL during the past decade is probably not due to the successful prevention of CNS leukaemia". To defend this notion, they might have compared the disease-free survival of patients who first relapsed in the CNS with that of the remaining patients. We are presented with the data for the former group (17/86, 20%) at 6 years, but not for the latter group. Only if this comparison reveals no significant difference can the controversial statement quoted above be regarded seriously.

That disease-free survival of the two groups may differ substantially might be inferred by comparing the marrow relapse rates for those patients with isolated CNS relapse versus the remaining group. The marrow relapse rate for patients with isolated CNS relapse was 60% (51/86) while for the remaining group, the proportion of patients with marrow relapse was about 30% at 5 years.[1]

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FEBRILE CONVULSIONS AND COT DEATH

SIR,—I was interested in the hypothesis of Dr Sunderland and Professor Emery (July 25, p. 176), in which they suggested that a relationship exists between febrile convulsions and cot death.

There is a definite genetic component in the cause of febrile convulsions so that when one child in a family is affected, the risk to a sibling is around 20%[1,2] and a heritability of 76% has been proposed.[1] With cot deaths the risk of recurrence is considerably smaller (possibly 2%)[4] and there is little hard evidence that genetic factors are of importance, although periodic breathing has been shown to be more common in siblings of cot death victims.[5] One way of pursuing the hypothesis put forward would be to ascertain whether cot death was more frequent than expected among siblings of children with uncomplicated febrile convulsions and vice versa.

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*** This letter has been shown to Dr Sunderland and Professor Emery, whose reply follows. ED. L.

SIR,—Since publication of our hypothesis we have received many letters. Some have suggested future epidemiological investigations. We would like evidence of both febrile convulsions and cot death occurring in the same family but our records are indexed by surname and the female half of the population tend to change their surnames before childbearing which therefore precludes an extended familial study. Children rarely convulse in the surgery so clinicians often have to take parental diagnoses at face value. We must treat death more circumspectly. There is an apparent discrepancy between the subsequent familial risk once a sibling has presented with either condition. Such relative risks appear to be partly dependent on the frequencies of the conditions. Ross et al.[1] have shown that the incidence of epilepsy after febrile convulsions among children in a community-based study who were not admitted to hospital was about half that found among those admitted to hospital or in other, hospital-based studies. Cot death studies are community-based whereas febrile convulsion studies are usually hospital-based and have the problem of an indeterminate, uncontrollable population at risk.

In addition to the problem of parental reporting of recurrence of convulsions, Peterson et al.[2] have shown that the mothers of families in which repeated cot deaths have occurred have significantly fewer full brothers and sisters than corresponding families without repeated cot deaths. If a statistician were able to correct for small family size would the familial recurrence risk of cot death rise?

If there is an association between some febrile convulsions and some cot deaths and if there are different physiological vulnerable periods for each, then it is an interesting speculation that a child who passes unscathed through the vulnerable period for cot death may later present as a febrile convulsion. We have been unable to devise a method to test this.

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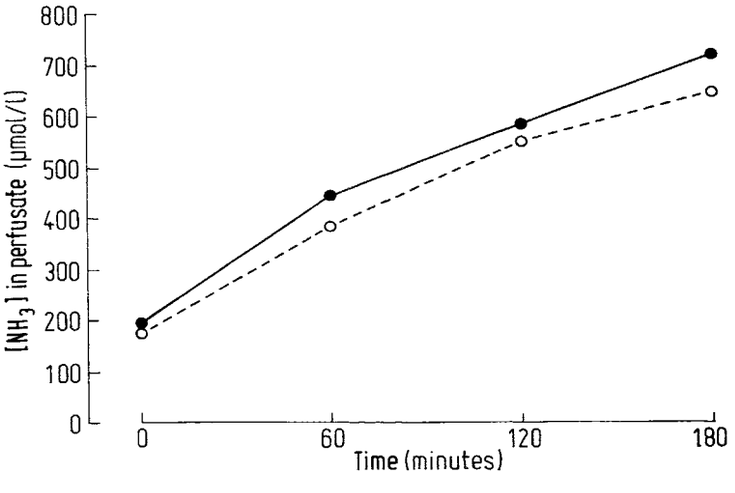
1. Robinson LL, Sather HN, Coccia PF, Nesbit ME, Hammond GD. Assessment of the interrelationship of prognostic factors in childhood acute lymphoblastic leukaemia: a report from Childrens Cancer Study Group. *Am J Pediat Hematol Oncol* 1980; **2**: 5–13.
2. Fukuyama Y, Kagawa K, Tanaka K. A genetic study of febrile convulsions. *Euro Neurol* 1979; **18**: 166–82.
3. Baraitser M. Clinical genetics: epilepsy. *Hospital Update* 1981; **7**: 139–47.
4. Peterson DR, Chinn NM, Fisher LD. The sudden infant death syndrome: repetitions in families. *Pediatrics* 1980; **97**: 265–67.
5. Kelly DH, Walker AM, Cahen L, Shannon DC. Periodic breathing in sibs of sudden infant death syndrome victims. *Pediatrics* 1980; **66**: 515–20.

ACTIVATED CHARCOAL AND AMMONIUM PRODUCTION

SIR,—When studying haemoperfusion as a tool for temporary artificial liver support we were surprised by the following observation. During in-vitro recirculation of 500 ml "coma mixture" (human albumin, aminoacids, short chain fatty acids, octopamine, ammonium chloride, and bile acids in physiological saline)[3] over 100 g uncoated activated charcoal (flow rate 100 ml/min, temperature 37°C) the ammonium concentration in the perfusate showed an almost linear increase with time (see figure). (Ammonium was determined with the 'Monotest Ammoniak', Boehringer Mannheim GmbH.)

This observation was extended in vitro by vigorous shaking of the different components of the coma mixture in the presence of uncoated charcoal ('Norit RBXI') at room temperature. Table I shows that the aminoacid mixture is the most important producer of

1. Ross EM, Peckham CS, West PB, Butler NR. Epilepsy in childhood: findings from the National Child Development Study. *Br Med J* 1980; **280**: 207–10.
2. Peterson DR, Chinn NM, Fisher LD. The sudden infant death syndrome: Repetitions in families. *J Pediatr* 1980; **97**: 265–67.
3. Chamuleau RAFM, Schoemaker LP, Smit EM. In vitro adsorption of possible aetiological factors of hepatic encephalopathy. *Int J Artif Organs* 1979; **2**: 284–88.



Ammonium concentration of coma mixture perfusate: two experiments.

TABLE I—AMMONIUM PRODUCTION BY COMPONENTS OF COMA MIXTURE

Medium	μmol NH_3/g coal/h
Coma mixture	0·42
Albumin (40 g/l)	0·0
Vamin (1: 200)	0·26
Octopamine (5 mg/l)	0·0
Octopamine, bile acids, Tau, Tyr	0·10

10 ml medium and 2 g coal shaken for 3 h at room temperature.

TABLE II—AMMONIUM PRODUCTION BY AMINOACID MIXTURES

Mixture		μmol NH_3/g coal/h	
		Coal	Coal + CA
Vamin	(0·05 g N/l)	0·59	0·11
Trophysan	(0·05 g N/l)	0·55	0·08
Aminosteril	(0·05 g N/l)	0·70	0·11
Aminess	(0·05 g N/l)	1·32	0·17

CA = cellulose acetate coating.

ammonium. When human plasma alone was shaken in the presence of uncoated charcoal ammonium production was 1·46 μmol/g coal/h, increasing to 1·99 μmol/g/h if 'Vamin' was added to plasma in a concentration of 0·05 g N/l.

Other commercial aminoacid mixtures show the same phenomenon (table II). Coating of the charcoal by cellulose acetate[4] diminishes ammonium production (table II). When the single aminoacid components of vamin were shaken in the presence of uncoated charcoal most of the ammonium proved to derive from L-methionine, L-tyrosine, and L-cysteine (respectively, 0·07, 0·05, and 0·08 μmol NH_3/g coal/h). Bacterial contamination as the source of NH_3 production was excluded since NH_3 production was the same under sterile conditions.

One of us (A. D.) suggested that the entrapped oxygen in the activated charcoal could be responsible for oxidation of these three aminoacids, thus making the aminogroup labile. Indeed when the activated charcoal was treated with nitrogen after vacuum extraction, ammonium production was almost zero in the presence of the aminoacid mixture.

This observation extends those of Tijssen[4] who has found that, in the presence of oxygen, creatinine and uric acid can be converted by activated charcoal in both unknown and known (ammonium, urea) products. Therefore we suggest that deoxygenation[5] is essential before activated charcoal is used in human haemoperfusion experiments, especially when the liver is failing.

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INTERFERENCE IN FLUORESCENCE/NEPHELOMETRY ASSAYS BY DIPYRIDAMOLE

SIR,—I should like to draw attention to the possibility of interference in certain laboratory tests by the drug dipyridamole ('Persantin'). When lipoproteins were being measured by a nephelometric method in this laboratory, it was noted that serum from a patient, subsequently found to be on treatment with dipyridamole, gave very high readings. The sample itself seemed clear (i.e., not turbid) but it did have a slightly fluorescent appearance to the naked eye in daylight and was more strongly fluorescent in ultraviolet light. Dipyridamole is a yellow crystalline powder, imparting a yellowish-blue fluorescence to solutions. The drug seems to be the likely cause of the anomaly because the nephelometer would measure the fluorescence. It is conceivable that dipyridamole could interfere in other laboratory tests involving fluorescence or nephelometry measurements.

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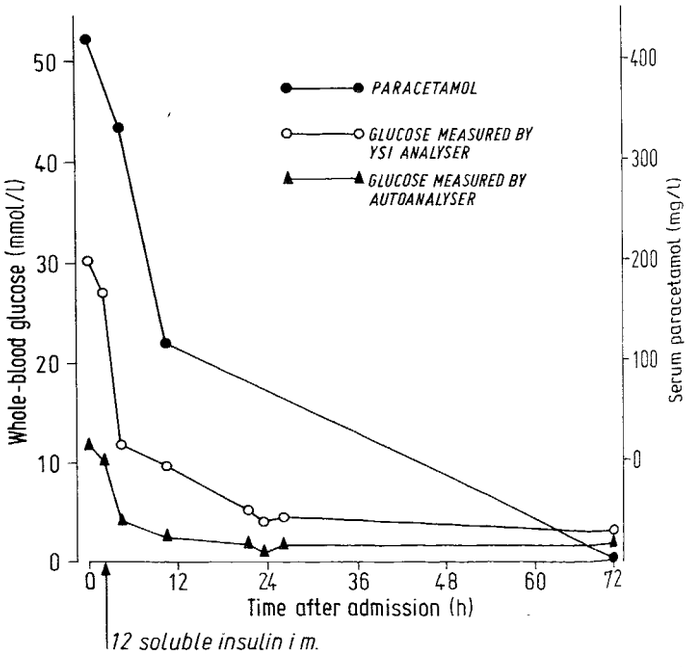
PARACETAMOL INTERFERENCE WITH GLUCOSE ANALYSIS

SIR,—Yellow Spring Instruments[1] say that high concentrations of paracetamol (acetaminophen) interfere with the performance of their glucose analyser, model 23 AM. Farrance and Aldons[2] suggest that the interference is greater than the manufacturers state, and I wish to report a case highlighting the hazards of such interference.

A young man was admitted in January, 1981, after paracetamol overdosage. Serum paracetamol was 534 mg/l (3.5 mmol/l) shortly after admission and 452 mg/l four hours later. The patient was treated with N-acetylcysteine. Routine urine analysis showed glycosuria and a sample of whole blood preserved with fluoride/oxalate was sent to the laboratory for glucose analysis. The blood glucose, measured by the YSI instrument, was reported as 30·2 mmol/l and the patient received 12 units of soluble insulin. Subsequent checking of the sample with an instrument using a different analytical principle gave a glucose of 12·5 mmol/l.

The accompanying figure shows the levels of glucose found by both systems in relation to the corresponding serum paracetamol: the discrepancy between the methods decreases as the paracetamol falls. When aqueous paracetamol solutions were tested in the YSI analyser, the amount of "glucose" detected was proportional to the amount of paracetamol. Solutions of paracetamol produced zero glucose levels with two other glucose methods which, like the method in the YSI analyser, employ glucose oxidase in the first stage of the analysis but which, unlike the YSI method, do not subsequently use potentiometry to measure the amount of hydrogen peroxide released. The two interference-free methods were the 'AutoAnalyzer' glucose oxidase method employing reagents from

1. Instruction manual YSI Model 23AM glucose analyser. Scientific Division Yellow Springs Instrument Co., Inc. Ohio, 1978
2. Farrance I, Aldons J. Paracetamol interference with YSI glucose analyser *Clin Chem* 1981; **27**: 782–83.



Serum paracetamol in relation to "whole-blood glucose" measured by two methods.

4. Tijssen J. A haemoperfusion column based on coated activated carbon. Ph.D. dissertation, Twente University, 1980.
5. Wieland H, Drishaus K. *Ann Chemie* 1934; **513**: 203.