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Cerebrospinal fluid acid-base status and lactate and pyruvate concentrations after short (< 30 minutes) first febrile convulsions in children

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SUMMARY Twenty-nine infants and children with short (<30 minutes) first febrile convulsions were studied between 3 and 22 hours after convulsive episodes. Arterial and CSF acid-base variables, lactate and pyruvate concentrations, and lactate/pyruvate ratios were measured. Biochemical signs of cerebral hypoxia were found in only 2 patients, one of whom had short, repeated convulsions. Our findings indicate that hypoxic damage is unlikely to result from a short-duration febrile convulsion.

Febrile convulsions affect some 6% of young children mainly between the ages of 6 months and 4 years. The long-term prognosis for such patients is usually good, though a small number, at most 5–10%, ultimately develop chronic epilepsy (see review by Lennox-Buchthal, 1973). Moreover, when the case records of adults with chronic epilepsy are scrutinized, a history of febrile convulsions in early childhood is often revealed. These observations have led to the postulate that seizures associated with fever, especially if prolonged, cause localized cerebral 'anoxic' damage and a predisposition to further convulsive episodes (Cavanagh and Meyer, 1956; Ounsted *et al.*, 1966; Falconer, 1971).

It seems important therefore to determine first whether first febrile convulsions of short duration (<30 minutes) result in cerebral hypoxia, detectable by alterations in cerebrospinal fluid (CSF) lactate and pyruvate concentrations and lactate/pyruvate ratios measured within 24 hours of the convulsive episode. The clinical usefulness of this biochemical approach in the detection of cerebral hypoxia has been shown in several earlier studies (Siesjö *et al.*, 1968; Granholm and Siesjö, 1970; Svenningsen and Siesjö, 1972; Blennow and Svenningsen, 1974). Here we present the results of studies in 29 patients. Those obtained in a further 22 children with convulsions of varied cause and duration (including 6 with prolonged or recurrent febrile convulsions) are given in the following paper (Simpson *et al.*, 1977).

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Patients

The 29 children with febrile convulsions and 14 'control' patients were studied in hospital. In each, including controls, there was a clinical indication for lumbar puncture. 1 ml CSF was obtained for analysis over and above that required for routine diagnostic purposes. Simultaneous radial arterial blood samples were also obtained in 20 of the patients with febrile convulsions. The nature and purpose of the investigation was explained to the parents of each child and their consent obtained.

Controls. Table 1 gives clinical details of the controls. The group comprised 14 children, 7 males and 7 females, of mean age 4·7 years (range 0·2–11·9 years). Of 6 with a previous history of convulsions, none had convulsed for at least one week before the study. 5 children were investigated because of meningism occurring during the course of acute respiratory tract infection or unexplained febrile illnesses. The remaining 3 gave a history of 'dizzy' spells for which no obvious cause was apparent. Normal CSF was obtained in each case. The patients in this group all recovered completely.

Febrile convulsions. Table 2 gives clinical details of the children with febrile convulsions. All were born between 36 and 42 weeks' gestation and 3 weighed less than 2500 g at birth (Cases 22, 30, 32). 4 had been moderately asphyxiated at birth but recovered after administration of oxygen by face mask (Cases

Table 1 *Clinical details of children selected as 'controls'*

Case no.	*Sex*	*Age (yrs)*	*Indications for lumbar puncture*	*Pyrexia†*
1	F	0·2	Unexplained fever	+
2	F	0·9	Suspected meningitis	+
3	M	1	Investigation convulsions*	—
4	M	1	,, ,,	—
5	M	1	,, ,, *	—
6	F	2	Suspected meningitis	+
7	M	3	Investigation convulsions*	+
8	M	4	,, ,,	—
9	F	4	Suspected meningitis	+
10	F	5	'Dizzy spells'	—
11	M	7	Suspected meningitis	+
12	F	10	'Dizzy spells'	—
13	F	11	Investigation convulsions	—
14	M	11	'Dizzy spells'	—

*Ketamine 5 mg/kg IM.
†Rectal temperature >38°C.

15, 21, 24, 31). A fifth was resuscitated by intubation and intermittent positive pressure ventilation and had recurrent cyanosis during the first day of life (Case 33). Previous psychomotor development had been normal in all but 2 patients—Case 19 in whom motor development was delayed and Case 15, thought by his parents to be unduly 'clumsy'.

A history of contact with infectious illnesses and/or immunizing procedures in the previous 4 weeks was obtained in 15 patients. Seizures were most often clonic in type and lasted less than 15 minutes. 3 patients (Cases 19, 23, 36) had brief recurrent convulsive episodes before the study. Fever was attributed to respiratory tract infection in 24 patients and to an infected tarsal cyst, gastroenteritis, urinary tract infection, and mumps in the remaining cases. Viral studies were carried out in all patients within 24 hours of admission to hospital. Positive

Table 2 *Clinical details of children with febrile convulsions*

Case no.	*Sex*	*Age (yrs)*	*Family* history*	*Contact or† immunization*	*Associated diagnosis*	*Convulsion‡*	*Approx duration (min)*	*Interval§ (h)*	*Medication‖*	*Virology*	*EEG***
15	F	1	—	Polio vaccination	LRTI	C	10	9	—	—	N
16	F	4	—	—	URTI	C	5	22	—	—	N
17	M	1	—	Measles contact	URTI	C	10	3	—	—	A
18	M	2	+	—	URTI	C	4	4	C	—	N
19	F	1	—	Rubella contact	URTI	C	3,3††	12‡‡	—	—	N
20	M	4	+	Rubella contact	Infected tarsal cyst	F	2	7	K	—	—
21	M	1	—	—	URTI	C	20	1	Th	—	—
22	F	4	+	Mumps contact	Mumps	C	10	9	K	Mumps	A
23	M	1	+	Polio, triple immunization	LRTI	C	7,5††	12‡‡	K	—	—
24	F	1	—	—	URTI	F	4	5	K	—	—
25	F	1	+	Triple immunization	URTI	C	5	16	K	Coxsackie A4	N
26	M	2	—	—	URTI	C	10	10	K	—	N
27	M	1	—	Smallpox vaccine	URTI	C	5	8	K	Parainfluenza 3	N
28	F	1	—	'Influenza' contact	LRTI	A	3	10	K		—
29	F	1	—	Measles vaccine	URTI	C	15	4	—	Parainfluenza 1	N
30	M	2	—	'Dysentery' contact	Enteritis	C	10	6	—	—	—
31	M	1	—	—	LRTI	A	3	4	—	Respiratory syncytial virus	—
32	M	1	—	—	URTI	T	15	6	K	Influenza A	N
33	M	2	—	'Influenza' contact	LRTI	A	1	5	—	Influenza A	—
34	M	2	+	—	URTI	C	4	5	K	Coxsackie A9	—
35	M	3	—	—	PUO	C	15	5	—	—	N
36	M	2	+	Measles vaccine	URTI	C	2	4	—	—	—
37	F	0·9	—	—	URTI	C	15	6	K	—	N
38	F	1	—	—	URTI	A	<10	5	—	—	N
39	M	1	—	Triple immunization	URTI	C	5	4	—	—	—
40	M	1	—	—	URTI	A	2,5††	6‡‡	K	—	—
41	F	1	+	Rubella contact	UTI	F	<30	5	—	Parainfluenza 3	—
42	M	2	—	—	URTI	C	9	4	Th	Adenovirus	N
43	M	4	—	—	URTI	T	2	3	K	—	N

*One or more febrile convulsions or epilepsy in first-degree relatives.
†Contacts with infectious illnesses and/or immunizing procedures in previous 4 weeks.
‡C = clonic; F = focal; T = tonic; A = akinetic.
§Interval between time of onset of convulsions and lumbar puncture.
‖C = chloral hydrate 500 mg orally; K = ketamine 5 mg/kg intramuscularly; Th = thiopentone 20 mg/kg rectally.
**At least 2 weeks after febrile convulsion episode. N = normal; A = abnormal.
††Two brief fits before lumbar puncture.
‡‡From onset of first convulsion.
LRTI, URTI = lower, upper respiratory tract infection; PUO = pyrexia of unknown origin; UTI = urinary tract infection.

isolates from throat and nasal swabs were obtained in 10 patients. Bacteria were also isolated in 10 patients: *Haemophilus influenzae* (5 cases), pneumococci and haemolytic streptococci from throat and nasal swabs, *Salmonella typhimurium* (2 cases) from stools, and *E. coli* from urine culture. Sterile CSF was obtained in every case. Electroencephalography was normal in 14 of 16 children investigated at least 14 days after convulsive episodes. Slight asymmetry was noted on the records of the remaining 2 (Cases 17, 22).

Procedure

Lumbar CSF and arterial blood samples were obtained simultaneously with the patient in the lateral recumbent position. CSF was collected in a 1 ml tuberculin syringe, care being taken to wash out dead space and to avoid air bubbles. Clear uncontaminated CSF was obtained in each case and the syringe capped immediately. Arterial samples were obtained by direct radial puncture with disposable no. 21 needles and withdrawn anaerobically into cold heparinized syringes over a 20-second period. In 3 patients in the control group and 13 with febrile convulsions, ketamine anaesthesia was used in a dosage of 5 mg/kg intramuscularly. Care was taken to ensure that the remaining patients were comfortable and breathing quietly during the procedure. Even so, it was not always possible to avoid disturbance during sampling.

Analytical methods

All measurements of *p*H and gas tensions in CSF and blood were made within 10 minutes of collection of samples. CSF *p*H was measured using a Radiometer glass electrode (G297/G2) and *p*H 22 meter used specifically for this purpose, and standardized with precision buffers (BDH *p*H 7·381 and *p*H 6·840). CSF was injected slowly into the proximal end of the electrode and care taken to avoid the formation of air bubbles. The electrode was flushed with CSF several times until two consecutive readings agreed to within 0·005 *p*H units. The total CO_2 content (Tco_2) of CSF was measured using the Natelson microgasometer (model 60). CSF Pco_2 and bicarbonate concentrations were calculated from *p*H and Tco_2 using the Severinghaus (1966) slide rule calculator. *p*H and Pco_2 were corrected to actual body temperature. The remaining CSF was used for determination of lactate and pyruvate. For lactate one volume of CSF (usually 0·1 ml) was added to two volumes 0·6 N perchloric acid; for pyruvate one volume of CSF (usually 0·5 ml) was added to an equal volume of N perchloric acid.

Arterial *p*H was measured using a Radiometer glass electrode (G297/G2) and PHM 27 meter standardized with precision buffers. Duplicate measurements agreed to within 0·005 *p*H units. Arterial Po_2 was measured by a Clark electrode (E/5046) calibrated daily with pure nitrogen and room air, and with the latter before and after each measurement. Duplicate measurements agreed to within 2 mmHg (0·27 kPa). Arterial Pco_2 was determined using the Severinghaus Pco_2 electrode (type E/5036) or by the Astrup equilibration technique. Calibrating gases had been analysed with Lloyd-Haldane apparatus to within $\pm 0{\cdot}02\%$. Arterial HCO_3 was calculated from the Henderson-Hasselbalch equation using the Severinghaus calculator (1966). *p*H and gas tensions were corrected to body temperature. Base excess was derived at the patient's actual haemoglobin from the Siggaard-Anderson (1963) alignment nomogram, and corrected for the *in vivo* effect of Pco_2 (Severinghaus and Bradley, 1968).

CSF and arterial lactate and pyruvate were measured by the Boehringer enzymatic method. For each a known standard was included with each batch of analysis and was used in the calculation of results.

Limitations of lumbar fluid measurements

The potential inaccuracies of using lumbar CSF to estimate the acid-base status of the brain in acutely ill patients have been described (Plum and Price, 1973; Plum, 1975). In conditions associated with severe cerebral hypoxia, lumbar CSF measurements underestimate the degree of acid-base derangement as reflected in cisternal CSF measurements (Kalin *et al.*, 1975). We considered, however, that the potential hazards of cisternal puncture precluded its use in routine practice.

Results

Clinical. Neurological examination carried out on admission and repeated in detail 24 hours later was abnormal only in one child (Case 38) who had a Todd's paresis for several hours during that period. Likewise total cell counts, sugar, and protein concentrations in CSF were within the normal range. After discharge from hospital each patient was assessed periodically for at least one year.

Controls. No attempt was made to obtain arterial blood samples in control patients. Table 3 gives the results of CSF acid-base variables, lactate and pyruvate concentrations, and lactate/pyruvate ratios. A mean *p*H of $7{\cdot}33 \pm 0{\cdot}03$, a mean Pco_2 of 44 ± 4 mmHg ($5{\cdot}87 \pm 0{\cdot}53$ kPa) lie within the range of

Table 3 *CSF acid-base variables, lactate and pyruvate concentrations, and lactate/pyruvate ratios in 'control' children*

Case no.	*pH*	*(H^+) (nmol/l)*	*Pco_2 (mmHg)*	*(HCO_3^-) (mmol/l)*	*Lactate (mmol/l)*	*Pyruvate (mmol/l)*	*$\frac{Lactate}{Pyruvate}$*
1	7·35	44·7	40	20·6	1·91	0·121	15·8
2	7·29	51·3	45	20·5	1·68	0·127	13·2
3	7·39	40·7	36	20·8	1·74	0·167	10·4
4	7·30	50·1	48	22·4	2·05	0·131	15·6
5	7·30	50·1	47	21·7	1·80	0·114	15·8
6	7·32	47·9	—	—	1·53	0·158	9·7
7	—	—	—	—	1·56	0·114	13·7
8	7·34	45·7	43	22·2	1·70	0·134	12·7
9	—	—	—	—	1·81	0·126	14·4
10	7·32	47·9	46	22·5	1·43	0·119	12·0
11	7·35	44·7	39	20·3	1·17	0·080	14·6
12	—	—	—	—	1·47	0·098	15·0
13	7·33	46·8	—	—	1·47	0·098	15·0
14	7·33	46·8	48	23·8	1·66	0·102	16·3
Mean	7·33	47·0	44	21·6	1·65	0·122	13·7
±SE	0·01	0·91	1·44	0·39	0·06	0·025	0·54
±SD	0·03	3·02	4·33	1·18	0·22	0·020	2·03
Range	7·29–7·39	40·7–51·3	36–49	20·3–23·8	1·17–2·05	0·080–0·16	9·7–16·3
n	11	11	9	9	14	14	14

Conversion: SI to traditional units—Pco_2: 1 kPa≈7·5 mmHg. HCO_3: 1 mmol/l = 1mEq/l. Lactate: 1 mmol/l≈9 mg/100 ml. Pyruvate: 1 mmol/l≈8·8 mg/100 ml.

normal values for adults (Huang and Lyons, 1966), children (Granholm and Siesjö, 1970), and newborn infants (Svenningsen and Siesjö, 1972; Krauss *et al.*, 1972). The mean bicarbonate of 21·6±1·2 mmol/l is slightly lower than published normal values, but compares with 'normal' control values reported by Plum and Price (1973). The lowest values are seen in 3 patients who were febrile when studied (Cases 1, 2, 11; Table 1).

The means ±SDs were lactate 1·65±0·22 mmol/l (14·9±1·98 mg/100 ml), pyruvate 0·122±0·020 mmol/l (1·07±0·18 mg/100 ml), and lactate/pyruvate ratio 13·7±2·03, which are similar to the results of Granholm and Siesjö (1970) in 10 children without evidence of neurological disease.

Febrile convulsions.

Acid-base variables.

Table 4 gives the results for arterial blood and CSF. In 20 patients with febrile convulsions arterial blood samples were obtained. The mean values ±SD were *p*H 7·40±0·04, Pco_2 30·3±4·0 mmHg (4·04±0·53 kPa), bicarbonate 18·4±2·1 mmol/l, and base excess −6·0±2·1 mmol/l. The mean Po_2 (16 patients) was 87±9·8 mmHg (11·60±1·3 kPa). In most cases there was mild to moderate metabolic acidosis resulting perhaps from fever, starvation, or convulsions *per se*. One child had diarrhoea (Case 27). Aspirin was not used in the treatment of these children in hospital but may have been given in a few cases before admission. The reduction in Pco_2 below 35 mmHg (4·66 kPa) in 16 patients is the result perhaps of mild metabolic acidosis, postictal hyperventilation, or, in some cases, disturbance associated with sampling procedures.

The mean CSF *p*H of 7·31±0·03 and Pco_2 of 42±5 mmHg (5·60±0·67 kPa) do not differ significantly from control values. The mean bicarbonate of 19·7±1·7 mmol/l is significantly lower than the mean bicarbonate of 21·6±1·2 mmol/l in controls ($0·05>P>0·02$).

When corresponding variables in blood and CSF are compared, (paired *t* test) CSF *p*H is significantly lower ($P<0·001$) and CSF Pco_2 higher ($P<0·001$) than in blood, which is the relationship normally found in adults (Bradley and Semple, 1962). CSF bicarbonate is significantly higher than arterial bicarbonate ($0·01>P>0·002$) which is the reverse of the normal relationship in adult men (Bradly and Semple, 1962). These findings are consistent with mild systemic metabolic acidosis (Albert *et al.*, 1966).

Lactate and pyruvate.

Table 5 gives the individual and group mean values and ranges of lactate and pyruvate concentrations and lactate/pyruvate ratios in blood and CSF of febrile convulsion patients. The means ±SDs were arterial blood lactate 1·44±0·53 mmol/l (13±4·8 mg/100 ml), pyruvate 0·114±0·040 mmol/l (1±0·35 mg/100 ml), and lactate/pyruvate ratio 13·1±2·85. Lactate concentration exceeded 2·0 mmol/l (18 mg/100 ml), the upper limit suggested by Oliva (1970) for nonfasting subjects, in 3 patients (Cases 19, 28, 33) and lactate/pyruvate ratio exceeded 16·0 in 3 cases (Cases 32, 41, 42). For each

Table 4 *Arterial blood and CSF acid-base variables in children with febrile convulsions*

		Blood					*CSF*			
Case no.	Po_2 (*mmHg*)	*pH*	H^+ (*nmol/l*)	Pco_2 (*mmHg*)	HCO_3 (*mmol/l*)	*Base excess* (*mmol/l*)	*pH*	H^+ (*nmol/l*)	Pco_2 (*mmHg*)	HCO_3 (*mmol/l*)
15	96	7·44	36·3	29	19·3	− 4·2	7·34	45·7	34	17·5
16	80	7·48	33·1	28	20·4	− 2·5	7·32	47·9	38	18·4
17	—	—	—	—	—	—	—	—	—	—
18	—	—	—	—	—	—	—	—	—	—
19	—	7·35	44·7	28	15·1	−10·1	7·28	52·5	43	18·6
20	—	7·34	45·7	36	18·8	− 5·8	7·29	51·3	40	18·2
21	76	7·37	42·7	30	16·1	− 8·0	7·29	51·3	48	21·8
22	—	7·40	39·8	26	15·8	− 8·4	7·34	45·7	37	19·0
23	79	7·42	38·0	28	18·0	− 6·2	7·35	44·7	36	19·0
24	102	7·38	41·7	35	20·4	− 4·0	7·27	53·7	46	20·0
25	66	7·42	38·0	30	19·2	− 4·8	7·34	45·7	40	20·5
26	80	7·39	40·7	29	17·2	− 7·2	7·30	50·1	40	18·6
27	82	7·42	38·0	26	16·6	− 7·3	7·27	53·7	39	16·9
28	—	7·35	44·7	39	21·2	− 3·5	7·30	50·1	44	20·6
29	—	—	—	—	—	—	—	—	—	—
30	—	—	—	—	—	—	7·31	49·0	37	17·3
31	—	—	—	—	—	—	7·33	46·8	40	20·0
32	91	7·38	41·7	29	16·7	− 8·0	7·28	52·5	46	20·1
33	98	7·36	43·7	34	18·8	− 5·9	7·33	46·8	45	22·1
34	89	7·43	37·2	27	17·5	− 6·2	7·33	46·8	39	19·0
35	92	7·38	41·7	28	16·2	− 8·6	7·33	46·8	43	21·3
36	—	—	—	—	—	—	—	—	—	—
37	100	7·38	41·7	38	22·1	− 2·3	7·34	45·7	42	21·6
38	—	—	—	—	—	—	—	—	—	—
39	—	—	—	—	—	—	—	—	—	—
40	85	7·44	36·3	26	16·9	− 6·2	7·30	50·1	41	19·1
41	91	7·40	39·8	31	22·5	− 5·6	7·24	57·5	59	23·8
42	83	7·44	36·3	28	18·8	− 5·2	7·31	49·0	40	19·1
43	—	—	—	—	—	—	7·26	35·0	47	19·9
Mean	87	7·40	40·0	30·3	18·4	− 6·0	7·31	48·6	42	19·7
±SE	2·44	0·01	0·75	0·89	0·48	0·47	0·01	0·92	1·09	0·35
±SD	9·75	0·04	3·37	3·99	2·14	2·08	0·03	4·42	5·23	1·68
Range	66–102	33·1–45·7	7·34–7·38	26–39	15·1–22·5	−10·0–2·3	7·24–7·35	44·7–57·5	34–59	16·9–23·8
n	16	20	20	20	20	20	23	23	23	23

Conversion: SI to traditional Units—Po_2: 1 kPa≈7·5 mmHg. Base excess: 1 mmol/l = 1 mEq/l.

of these variables, however, values were scattered within a fairly wide range.

CSF lactate concentration was 1·75±0·31 mmol/l (15·8 ± 2·8 mg/100 ml), pyruvate 0·122 ± 0·17 mmol/l (1·07±1·5 mg/100 ml), and the lactate/pyruvate ratio 14·6±2·5, which do not differ significantly from the control values given in Table 3. This is also true for control data computed for children within the febrile convulsion age range (Cases 1–9, Table 3). Lactate concentration exceeded 2·1 mmol/l (18·9 mg/100 ml) (the upper limit for controls) in 4 patients (Cases 19, 27, 28, 38), and the lactate/pyruvate ratio exceeded 18·0 in 3 (Cases 19, 30, 38). In 2 patients there was an increase in both lactate concentration and lactate/pyruvate ratio (Cases 19, 38).

When arterial blood and CSF are compared, lactate concentration was significantly higher in CSF ($0·02>P>0·01$), as was the lactate/pyruvate ratio ($0·05>P>0·02$). Pyruvate concentrations in blood and CSF were not significantly different. Although the changes in CSF were small and could not be expected to influence acid-base variables, there was a significant inverse correlation between CSF lactate and hydrogen ion concentration ($0·05>P>0·02$). No relation was found between CSF lactate and CSF or arterial Pco_2 or CSF bicarbonate.

Ketamine. 16 children, 13 in the febrile convulsion group, were given ketamine. There were no significant differences in the measured blood or CSF variables in these patients and those not given ketamine within either the control or febrile convulsion groups.

Discussion

Metabolic changes during and after brief epileptic seizures have frequently been studied in adult man (Meyer *et al.*, 1966; Posner and Plum, 1968; Posner *et al.*, 1969; Brodersen *et al.*, 1973) and in experimental animals (Gurdjian *et al.*, 1946; King *et al.*, 1967, 1970; Plum *et al.*, 1968; Collins *et al.*, 1970). These and other studies have shown that during major generalized convulsions there is an increased

Table 5 *Arterial blood and CSF lactate and pyruvate concentrations and lactate/pyruvate ratios after febrile convulsions*

	Blood			*CSF*		
Case no.	*Lactate (mmol/l)*	*Pyruvate (mmol/l)*	*Lactate / Pyruvate*	*Lactate (mmol/l)*	*Pyruvate (mmol/l)*	*Lactate / Pyruvate*
15	1·33	0·138	9·7	1·59	0·102	15·6
16	1·17	0·109	10·7	1·85	0·122	15·2
17	—	—	—	1·38	0·088	15·7
18	—	—	—	1·88	0·172	10·9
19	2·62	0·167	15·7	2·10	0·099	21·2
20	1·21	0·082	14·7	1·85	0·108	17·1
21	1·48	0·099	15·0	1·71	0·098	17·5
22	0·98	—	—	1·35	0·108	12·5
23	0·83	0·076	10·9	1·77	0·117	15·2
24	1·00	0·065	15·4	1·44	0·100	14·4
25	1·41	0·097	14·6	1·24	0·105	11·8
26	0·90	0·082	11·0	1·45	0·129	11·2
27	1·71	0·162	10·6	2·35	0·147	16·0
28	2·34	0·180	13·0	2·15	0·148	14·5
29	—	—	—	1·79	0·104	17·2
30	—	—	—	1·96	0·105	18·7
31	—	—	—	1·90	0·169	11·3
32	1·08	0·064	16·9	1·56	0·117	13·3
33	2·17	0·196	11·1	1·80	0·128	14·1
34	0·88	0·113	7·8	1·42	0·122	11·6
35	0·94	0·072	13·0	1·61	0·115	14·0
36	—	—	—	1·56	0·109	14·3
37	1·97	0·151	13·1	1·28	0·109	11·7
38	—	—	—	2·53	0·136	18·6
39	—	—	—	1·63	0·129	12·6
40	1·34	0·125	10·7	1·99	0·148	13·4
41	1·96	0·116	16·9	1·97	0·130	15·1
42	1·41	0·071	17·8	1·88	0·126	14·9
43	—	—	—	1·87	0·136	13·7
Mean	1·44	0·114	13·1	1·75	0·122	14·6
±SE	0·12	0·009	0·64	0·06	0·003	0·47
±SD	0·53	0·040	2·85	0·31	0·017	2·52
Range	0·38–2·62	0·064–0·196	7·8–17·8	1·24–2·53	0·088–0·172	11·9–21·2
n	20	19	19	29	29	29

demand for cerebral energy production with an increase, often several fold, in cerebral metabolic rate. At the same time the energy supply to the brain is reduced due to impairment of pulmonary ventilation and increased metabolism of muscle during the tonic phase of seizures. As a consequence of oxygen depletion, there is a rapid fall in cerebral tissue high energy phosphates and a rise in lactate. The latter is reflected in the CSF where lactate may remain raised for several hours, probably quite independent of blood lactate concentrations (Posner and Plum, 1967).

A great deal of experimental work has been concerned with the theoretical validation of CSF lactate concentration and lactate/pyruvate ratios as possible indices of brain hypoxia. Either variable can be influenced by intracellular acid-base balance, which must be considered to avoid misinterpretation. Many of the metabolic consequences of tissue hypoxia will increase lactate production by increasing the rate of glycolysis. However, an increase in lactate with a proportionate increase in pyruvate has been shown experimentally during alkalosis, when hypoxia is not present (Delcher and Shipp, 1966; Leusen and Demeester, 1966). The concept of using lactate/pyruvate ratio as a more reliable indicator of hypoxia (Huckabee, 1958; Hohorst *et al.*, 1969) was based on the knowledge that lactate and pyruvate diffuse freely through most cell membranes and that the lactate/pyruvate system is coupled in an equilibrium reaction to the cytoplasmic NADH/NAD$^+$ system. Thus increased production caused by hypoxia leads to an increase in lactate/pyruvate ratio. However, it has been shown that an increase in lactate/pyruvate ratio and NADH/NAD$^+$ may also result from acidosis *per se* (Granholm and Siesjö, 1969; Messeter and Siesjö, 1971; Siesjö *et al.*, 1971) and in this situation lactate concentration is usually decreased. It seems therefore that an increase in both lactate concentration and lactate/pyruvate ratio probably occurs only in hypoxia and that these changes reflected in cerebrospinal fluid may be the earliest signs of tissue oxygen lack.

The present results have shown that CSF lactate concentration and lactate/pyruvate ratios are not increased in the majority of infants and young

children studied within 24 hours after first-time short-duration febrile convulsions. The absence of changes in CSF lactate and lactate/pyruvate ratios in the majority of cases probably means that clinically obvious hypoxia (indicated by the occurrence of cyanosis during convulsions) was not associated with cerebral hypoxia. Alternatively, there may have been rapid resorption and metabolism of such minute amounts of lactate and pyruvate that could have been produced in the immediate post convulsive period. Only 2 patients in the present series (Cases 19, 38) showed signs of cerebral hypoxia with an increase in both CSF lactate concentration and lactate/pyruvate ratio above the upper limit for values obtained in controls. Of these, Case 19 had two brief grand mal seizures before sampling, and Case 38 had a tonic convulsion lasting less than 10 minutes. Both children had upper respiratory tract infections, but in neither case was a virus isolated. The possible prognostic significance of findings in these children will only become apparent after a further follow-up period. Our results are therefore in general agreement with those of Blennow and Svenningsen (1974) who were unable to detect biochemical signs of hypoxia using the same indices in 20 children studied between 10 minutes and 9 hours after a sustained febrile convulsive episode. We conclude also that hypoxic brain damage is unlikely to result from a short-duration febrile convulsion.

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