Hypernatraemia as a cause of intracranial haemorrhage

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Roberton, N. R. C., and Howat, P. (1975). *Archives of Disease in Childhood,*
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finite intracranial haemorrhages and 4 suspected ones occurred during a 25-month
period during which 10 072 live infants were born. There were 4 subdural haemor-
rhages (all fatal), 4 isolated subarachnoid haemorrhages (2 fatal), and 21 intraventricular
haemorrhages (all fatal—2 beyond the neonatal period). There was no evidence of a
causal relation between intraventricular haemorrhage and either hypernatraemia or
large sodium intakes. There were too few cases of other types of intracranial
haemorrhage to draw any aetiological conclusions.

The recent study by Simmons *et al.* (1974)
suggested that the restricted use of sodium bicarbo-
nate in 1970–1971 was associated with a lower
incidence of intracranial haemorrhage (ICH) when
compared with more liberal use of bicarbonate in
1966–1967. Volpe (1974), in an accompanying
editorial, pointed out that many of their conclusions
were not justified, and Cole *et al.* (1974), in their
more detailed study restricted to intraventricular
haemorrhage (IVH), were unable to document such
an association. We have therefore reviewed our
experience over a 25-month period ending 31 July
1974 to see if we could establish any relation
between hypernatremia and ICH.

Material and methods

Our routine management of sick low birthweight
infants has been described (Davies *et al.*, 1972). All
such infants have indwelling umbilical arterial catheters,
and because of the risk of apnoea following THAM
(Roberton, 1970), sodium bicarbonate was the base
routinely used. Boluses of the 8·4% solution were
infused when necessary at approximately 1 ml/min to
maintain pH_a 7· ≥25. Blood was analysed for sodium
at least daily, and the sodium intake in mEq/kg per 24 h
was calculated from the sodium intake in milk (Shaw,
Jones, and Gunther, 1973) plus the amount given
intravenously as bicarbonate or dextrose saline.

We maintained our umbilical artery catheters with
heparinized saline (10 μm/ml). After use, catheters
were cleared by infusing 50% more heparinized saline
than the internal volume of the catheter; 0·1 ml of
saline (containing 0·015 mEq Na) would therefore be
infused every time the catheter was used. This quan-
tity has been ignored in our calculations of sodium intake.

Results

We examined the records of infants who were
born in the hospital who had (a) developed hyper-
natraemia (Na ≥150 mEq/l) during the neonatal
period, (b) received more than 8 mEq/kg during
any 24 hours in the neonatal period, (c) developed
any form of ICH detected clinically or at necropsy
during the neonatal period.

During the study period 10 072 infants were born,
and 1501 were admitted to our special care baby
unit. 50 nonmalformed infants died, 44 had
necropsy examinations, and 25 of these had some
form of ICH. 4 were subdural haemorrhages,
2 were subarachnoid haemorrhages alone, and 19
were IVH. 2 surviving infants were diagnosed as
having subarachnoid haemorrhages, and 2 other
infants died later in infancy after a shunt operation
for posthaemorrhagic hydrocephalus attributed to a
neonatal IVH.

Four of the 6 infants who did not have a necropsy
examination were thought on clinical evidence to
have had an IVH. The birthweights of infants
with IVH are given in Table I. 14 infants de-
veloped hypernatraemia, and 38 received more than
8 mEq Na/kg per 24 h. Their birthweights are
given in Table II. The inter-relation between
hypernatraemia, high sodium intake, and ICH is
shown in Fig. 1. 12 of the 21 infants with IVH
received more than 8 mEq Na/kg per 24 h, 4 of the
21 were hypernatraemic, but only 2 infants were
hypernatraemic, received a high sodium intake, and
had an ICH.

We also investigated the relation between
IVH, hypernatraemia, and high sodium intake in all

TABLE I

Cases of IVH

Birthweight (kg)	IVH at necropsy	Clinical course suggesting IVH (no necropsy)	No. live born	% with IVH
<1·0	5	1	14	42·9
1·0 kg—<1·5	8*	3	57	19·3
1·5 kg—<2·0	7	–	131	5·8
>2·0	1	–	9870	0·01

*Including 2 infants dying after the neonatal period with hydrocephalus and evidence of an old IVH.

TABLE II

Incidence of hypernatraemia and high sodium intake at different birthweights

Birthweight (kg)	≥8 mEq/kg per 24 h		Hypernatraemia ≥150 mEq/l	
	Alive	Dead	Alive	Dead
<1·0	1	5	–	4 (2)
1·0—<1·5	4	7	4 (1)	–
1·5—<2·0	2	7	1	1
2·0—<2·5	2	2	1	–
>2·5	2	6	6	1 (1)

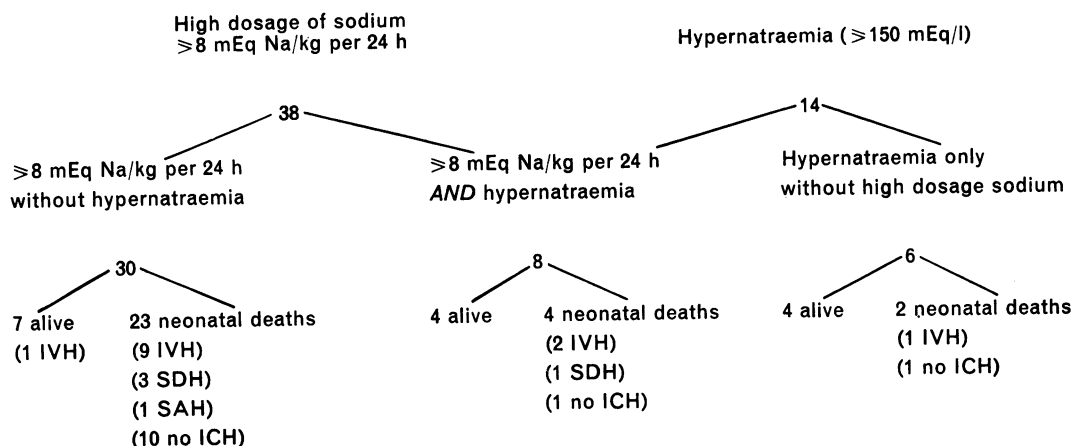Figures in parentheses = Na ≥160 mEq/l.

FIG. 1.—*Relation between ICH, hypernatraemia, and sodium administration at all birthweights. 8 infants with IVH and 3 with SAH were neither hypernatraemic nor received ≥8 mEq Na/kg per 24 h. SAH, subarachnoid haemorrhage; SDH, subdural haemorrhage; IVH, intraventricular haemorrhage; ICH, intracranial haemorrhage.*

infants between 1·0 and 2·0 kg (Fig. 2 and 3). IVH was present in 15 of the 188 infants (8·0%), and in 15 of the 21 nonmalformed infants on whom a necropsy was performed (68%). There is no relation apparent between either factor and IVH. Furthermore, 6 of the 9 dead infants with IVH in the >8 mEq Na/kg per 24 h group received their sodium after the collapse attributed to the IVH.

The clinical details of the infants with subdural and subarachnoid haemorrhages are given in Table III. All of the infants with subdural haemorrhages were severely asphyxiated and 3 had associated tentorial tears. Only one of the infants with subarachnoid haemorrhage received high doses of sodium, and he was critically ill with a group B β-haemolytic streptococcal septicaemia.

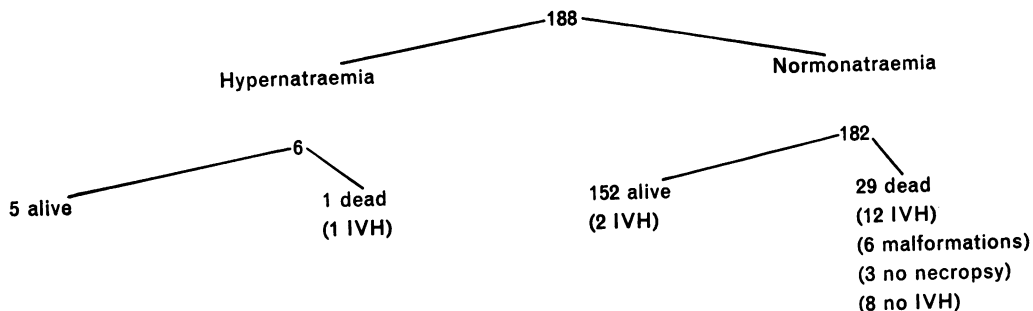3 of the hypernatraemic infants had fits; 1 survived—an infant with a maximum sodium of 163

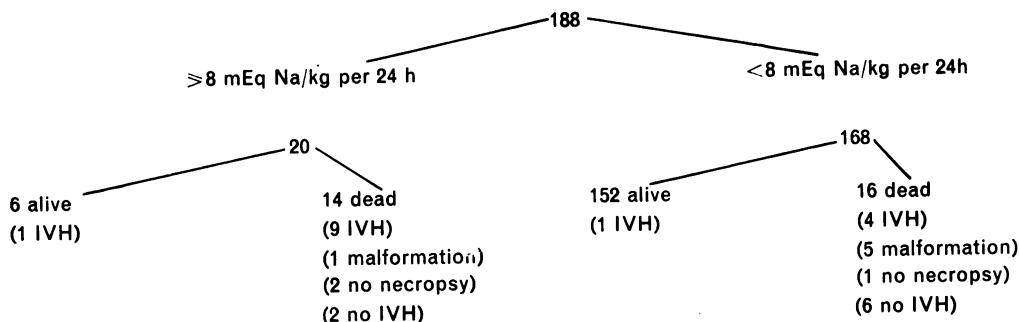3

FIG. 2.—*IVH in infants developing hypernatraemia.* $1 \cdot 0 – 2 \cdot 0$ *kg birthweight only.*

FIG. 3.—*Infants receiving* $\geqslant 8$ *mEq Na/kg per 24 h.* $1 \cdot 0 – 2 \cdot 0$ *kg birthweight only.*

TABLE III
Infants with subdural (SDH) and subarachnoid (SAH) haemorrhage

Case no.	Birthweight (kg)	Gestation (w)	Type of haemorrhage	$\geqslant 8$ mEq Na/kg per 24h	Na $\geqslant$ 150 mEq	Diagnosis
1	3·81	40	SDH	+	—	Died; birth asphyxia; tentorial tear
2	0·99	26	SDH	+	—	Died; tentorial tear
3	3·88	39	SDH	+	—	Died; severe birth asphyxia
4	1·70	36	SDH	+	—	Died; tentorial tear; HMD, severe bronchopulmonary dysplasia
5	1·95	36	SAH	—	—	Alive; arrested hydrocephalus normal developmental progress
6	2·70	37	SAH	—	—	Alive; Rhesus haemolytic disease
7	1·62	22	SAH	—	—	Died; *Esch. coli* septicaemia; internal hernia
8	2·98	38	SAH	+	—	Died; Group B β-haemolytic streptococcal septicaemia

mEq/l. The fits in this infant were probably due to the hypernatraemia. The two other hypernatraemic infants with fits were a severely asphyxiated term infant, and a 800 g 26-week premature who had a horseshoe kidney and a massive IVH. 8 other infants who had IVH developed tonic fits terminally. All received high doses of sodium, but none were hypernatraemic.

Discussion
ICH is a major cause of neonatal death, but in any analysis of neonatal ICH it is very important to consider IVH in a separate category. The aetiology of IVH remains uncertain. However, its association with extreme prematurity has led most workers to conclude that hypoxia plays a major role. The capillaries in the highly vascular

germinative zone overlying the basal ganglia are very susceptible to vascular stasis, thrombosis, rupture, and haemorrhage. In a sick infant this tendency may be aggravated by the increased capillary fragility of hypoxia and acidaemia, surges in central venous pressure, or arterial blood pressure coagulation disturbances, and perhaps by rapid alterations in plasma osmolarity (Cole *et al.*, 1974; Hambleton and Wigglesworth, 1975.)

IVH is primarily a condition of very low birthweight infants (Table I) (Fedrick and Butler, 1970), and is very rare in infants weighing more than 2·0 kg; the only such case in our series being an infant with an undiagnosed blood dyscrasis presenting shortly after birth with massive haemolysis, jaundice, thrombocytopenia, and petechial haemorrhages not due to fetal infection.

During the period of our study we have not changed our indications for giving bicarbonate. We are therefore not in a position to comment on a different incidence of IVH associated with decreasing use of intravenous base. However, we have found no correlation between sustained hypernatraemia and IVH, though the incidence of transient hypernatraemia will have been underestimated. Infusions of base cause transient surges of osmolarity which return to normal within 15 minutes (Baum and Roberton, 1975). We have also failed to show any association between large doses of sodium and IVH. The higher mortality rate in infants receiving large amounts of sodium was due to the severity of the illness since the lower the *p*H the larger the dose of sodium bicarbonate administered.

There may be several reasons for the different conclusions drawn by Simmons *et al.* (1974) and ourselves. Each type of neonatal ICH has a differing aetiology and pathogenesis. By considering all types of ICH together Simmons *et al.* (1974) may have masked the fact that there was no association between hypernatraemia and IVH. Infusions of hypertonic solutions which are prolonged or more rapid than 1 ml/min may cause ICH of the subdural subarachnoid, or petechial type but very rarely cause IVH (Luttrell and Finberg, 1959; Luttrell, Finberg, and Drawdy, 1959). Simmons *et al.* (1974) state that there was no evidence of trauma in their cases of subdural haemorrhage, so that these, and their cases of subarachnoid and petechial haemorrhage, may well have been due to overexuberant use of base. However, we had no cases with brain stem petechial haemorrhage, and our cases of subdural and subarachnoid haemorrhage were not due to excessive bicarbonate administration, since the infants either received no bicarbonate or received

it after the damage was done by streptococcal septiceaemia or intrapartum asphyxia with a tentorial tear (Table III).

A number of other factors may have contributed to their reported decrease in ICH as a whole. They do not give details of the birthweight distribution of their nursery population in the two periods studied, nor the incidence of neonatal illnesses known to predispose to ICH of any form.

Furthermore, ICH, hypernatraemia, and large sodium intake, though present in the same infant, may not be causally related. Thus, after an IVH an infant becomes apnoeic, hypoxic, acidaemic, and shocked. In a vain attempt to resuscitate such infants large quantities of base may be given. In 6 of the 9 cases of IVH in our series where >8 mEq Na/kg per 24 h was given, it was given *after* such a collapse. In the other 3 bicarbonate was given partly for severe birth asphyxia and partly after the collapse attributed to the IVH. In infants with subdural haemorrhage an apparent association with hypernatraemia could also be explained by the base being given after a severely asphyxial delivery causing a tentorial tear.

Since we have failed to show any association between hypernatraemia, large sodium intake, and IVH, we feel that it is important to stress that infusions of base should not be withheld from acidemic infants because of an uproven risk of IVH. When a large base deficit is present after severe birth asphyxia, cardiac arrest, or severe apnoeic attacks, base should be given at a rate no faster than 1 mEq/min (Baum and Roberton, 1975). For the premature infant at risk from hyaline membrane disease, the prevention of acidaemia is particularly important since surfactant synthesis is *p*H-dependant (Gluck *et al.*, 1972). However, by not attempting correction to greater than *p*H 7·25, and by adequate maintenance of Pao_2, haematocrit, and blood volume (Roberton, 1975) the use of base subsequently can and should be minimized.

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