Witness Statement Ref. No. 350/2

NAME OF CHILD: CONOR MITCHELL

Name: Dr. Darrell Lowry

Title: Consultant Anaesthetist

Present position and institution:

Consultant Anaesthetist, Southern HSCT

Previous position and institution: Consultant Anaesthetist, Craigavon Area Hospital
[As at the time of the child's death]

Membership of Advisory Panels and Committees:
[Identify by date and title all of those since your last witness statement]

NI Sick Child Liaison Group 2000 – 2004
NI Paediatric Anaesthesia Group 2000 – present
NI Working group on hyponatraemia in children 2001
NI Paediatric Neonatal retrieval service working party 2003- 2004
Paediatric Resuscitation Committee Craigavon Area Hospital 2000 – 2012
Chair Medical Staff Committee Craigavon Area Hospital 2009 -2012
NIMDTA Anaesthetic Training Committee 2002 – present
Southern Trust Local Negotiating Committee 2007 - present
BMA Northern Ireland Consultants Committee 2009 – present
RCoA e Portfolio working group 2009 – 2012
RCoA Assessment working group 2009 – present
RCoA National Recruitment Committee 2012 – present
RCoA ni Advisory Board 2009 - present

Previous Statements, Depositions and Reports:
[Identify by date and title all those made in relation to the child's death]

WS 350-1 (20-09-13)

OFFICIAL USE:
List of previous statements, depositions and reports attached:

Ref:	Date:	

IMPORTANT INSTRUCTIONS FOR ANSWERING:

Please attach additional sheets if more space is required. Please identify clearly any document to which you refer or rely upon for your answer. If the document has an Inquiry reference number, e.g. Ref: 049-001-001 which is 'Chart No.1 Old Notes', then please provide that number.

If the document does not have an Inquiry reference number, then please provide a copy of the document attached

(1) Please confirm that in or about 2001 you worked with Dr. Mike Smith (Consultant Paediatrician) and Dr. Peter Sharpe (Consultant Biochemist) as part of an informal group to develop guidance on the prevention and management of hyponatraemia in children.

I recall working with Dr Smith but not Dr Sharpe.

If so, please address the following matters:

(a) Identify the person who appointed you to this group or asked you to participate in it.

I do not recall that anyone actually asked me to participate.

(b) Identify any other person (apart from those named above) who was appointed to this group, or who was asked to participate in it or assist it in its work.

None that I recall.

(c) Describe in detail what you and the other members of this group were asked to do.

I do not recall being asked to do anything.

(d) Insofar as you are aware, describe the circumstances in which it was deemed important to bring together an informal group to develop guidance on the prevention and management of hyponatraemia, or otherwise explain the reason for the decision to constitute this informal group.

I was a member of the September 2001 working group on hyponatraemia in children and so was aware of the potential problem in our hospital as well as across the Province. As Lead Consultant Paediatric Anaesthetist in Craigavon I felt it was my role to take this forward and development guidelines in conjunction with a Consultant Paediatrician (Dr Smith). I had worked in RBHSC before taking up my Consultant post in Craigavon and was aware of the Arieff paper. After Dr Nesbitt telephoned me describing the death of his patient in Altnagelvin I felt it important to develop guidelines to prevent the same event occurring in Craigavon.

(e) Describe the work which you and this group carried out, and explain how this work was carried out.

From memory, Dr Smith and I met once or twice in our offices and then had e mail correspondence to come up with the guidelines.

(f) Provide a copy of any policy, guidance, procedure, protocol, advice or any other output of this group. If you do not hold a copy of any such document, please provide a detailed description of the output of this group.

These are attached to this statement.

(g) Specify the date or the approximate date when this group completed its work.

Around the end of 2001. The DHSS guidelines then came out in 2002.

(h) When this group completed its work, who did it report to?

I do not recall reporting to anyone. The guidelines were put on the hospital intranet.

(2) Since completing your work as part of the informal group referred to at 1 above, have you undertaken any other work in the Craigavon Area Hospital of the following kind:

(a) The development of advice or guidance in relation to the management of hyponatraemia;

Not to my knowledge.

(b) The production of protocols or procedures in relation to the management of intravenous fluids;

Not to my knowledge.

(c) The provision of education, training or induction to nursing staff, medical staff or trainees in relation to issues surrounding hyponatraemia and fluid management;

I gave regular lectures to theatre, recovery and Day Surgery Unit nursing staff on paediatric anaesthesia which included mention of paediatric fluid management. One of my anaesthetic registrars gave a talk on hyponatraemia at the hospital Friday lunchtime postgraduate clinical meeting in July 2001. This was open to all medical staff in the hospital. I also talked to ENT medical staff about fluid management in children.

(d) The conduct of audits in relation to compliance with guidance or protocols applicable to fluid management and the management of hyponatraemia.

If you have undertaken any work of the kind described above, please address the following matters:

(i) Describe the work you carried out;

I did a retrospective chart audit of children having an appendicectomy in Craigavon Area Hospital from April - July 2001. This audit was undertaken prior to either local or regional guidelines being issued.

(ii) Identify any other person you worked with in carrying out this work;

No one else.

(iii) Identify the person who asked you to carry out the work, and the person who you were asked to report to upon the completion of the work;

It was my own idea and my own work.

(iv) State the date or approximate date when the work was carried out and completed;

I cannot find my presentation but from my notes it is probably around about September 2001.

(v) Provide copies of any document produced in the completion of such work. If you do not hold a copy of any such document, please provide a detailed description of the document.

I cannot find my powerpoint presentation however I attach my handwritten summary. Eleven patents were audited with ages ranging from 3 - 13 years (mean 10 years). In 6 out of 11 cases the appropriate fluids were given both pre and post operatively. Nine children had a pre-op U&E with the sodium ranging from 132 - 139 mmol/l. Five patients received No. 18 solution pre-operatively; only one patient received post-operative No. 18 solution. I presented this audit at an anaesthetic audit meeting in Craigavon Hospital.

(3) The Chief Medical Officer published 'Guidance on the Prevention of Hyponatraemia in Children' in or about March 2002. The correspondence which explained the purpose of this Guidance was addressed to Consultant Anaesthetists amongst others (Ref:007-001-001).

Please address the following matters arising out of this correspondence:

(a) Did you receive a copy of this correspondence in your capacity as Consultant Anaesthetist in Craigavon Area Hospital?

I'm sure that I did but I cannot recall with certainty.

(b) The CMO's correspondence indicated that the A2 sized poster describing the Guidance should be displayed in all units which accommodated children. Insofar as it is within your knowledge, specify the locations within Craigavon Area Hospital where the poster was displayed.

I remember it being displayed in main theatres, theatre recovery and the Day Surgery Unit.

(c) The CMO's correspondence indicated that local fluid protocols should be developed to complement the Guidance. Did you formulate any such protocols or did you work with or use any such protocols? If so, identify the relevant protocol, and provide a copy of same.

We already had our protocol in place from 2001.

(d) The CMO's correspondence stated that it would be important to audit compliance with the Guidance and the locally developed protocols. Did you carry out any such audit or was your work or the work of your department the subject of any such audit insofar as you are aware? If so, provide full details of the audit which was carried out, and the results or conclusions produced by the audit.

I cannot recall, however fluid balance chart audits were regularly carried out in Craigavon. I have attached minutes from an audit meeting detailing one such audit.

(e) Did you take any steps whether individually or as part of a group to take this Guidance forward within Craigavon Area Hospital? If so –

I cannot recall any steps taken.

(i) Describe in detail all of the steps that you took in order to take the Guidance forward within Craigavon Area Hospital;

(ii) Identify any other person who worked with you on this task;

(iii) Identify the person who asked you to carry out this work, and the person you reported to.

(4) You are referred to the document at Ref: 329-014-057, -058 and -059 entitled *'Hyponatraemia in Children'* ("the document")

As appears from the screen print at Ref: 329-014-060, the document at Ref:329-014-057 and following was produced by the Royal Group of Hospitals in September 2001.

The Inquiry is advised that the document was then included in trainee anaesthetist induction packs at Craigavon Area Hospital.

Please address the following matters:

(a) Insofar as you aware fully describe the circumstances in which the document was supplied to Craigavon Area Hospital?

I cannot remember exactly but I think that it was sent to me by Dr Bob Taylor as I was a member of the hyponatraemia working group. I may have asked him to send it to me personally but I cannot remember.

(b) Insofar as you are aware identify the person who supplied the document to Craigavon Area Hospital.

Either Dr Taylor or Dr M McCarthy from the DHSS.

(c) Did you engage in any discussions with clinicians at the Royal Belfast Hospital for Sick Children in relation to the management of hyponatraemia, or hyponatraemia deaths in Northern Ireland, whether before or after the document was supplied to Craigavon Area Hospital?

If so, fully describe the discussions which you had and who you had them with.

I was a member of the NI Paediatric Anaesthetic Group. I remember attending a meeting of this group in Musgrave Park Hospital at which the case of a child from Altnagelvin (whom I now know to be Raychel Ferguson) was presented by Dr G DiMascio, Consultant Anaesthetist, Altnagelvin Hospital. I have no record of the minutes of this meeting however from WS-038/1 p14 it seems to have taken place in November 2001.

(d) Insofar as you are aware, fully describe the circumstances in which it was decided that it was necessary to include information regarding hyponatraemia in children in induction packs for trainee anaesthetists, and identify the person(s) who made this decision and the date or the approximate date when the decision was made.

As far as I am aware, I made the decision to include the information. This is because of my involvement in the NI working group on hyponatraemia in children. I wanted to stress the importance of the potential for hyponatraemia in these patients and to educate our trainees in order to prevent any further deaths, either in Craigavon or elsewhere.

THIS STATEMENT IS TRUE TO THE BEST OF MY KNOWLEDGE AND BELIEF

Signed: Damian O'Hare **Dated:** 19.09.13

CAM

Intravenous Fluids in Children

Revised: 11 October 2001

Dilutional hyponatraemia has been documented in otherwise healthy children following routine elective surgery. It occurs in (often female) children 3-10 years of age and is associated with "stress" such as postoperatively.

A fluid for children recommended for many years as a standard is 0.18 NaCl in 4% Glucose. It contains 40 mmol/l of sodium which when administered at the calculated rate (4 mls/kg/hour for the first 10 kgs body weight) provides the daily requirement of sodium and glucose.

0.18 NaCl in 4% Glucose is **isotonic** *in vitro* ie has the same osmotic potential so will not cause fluid shifts within the body. However in the catabolic (sick) child the glucose is metabolised rapidly causing the fluid to become ***hypotonic*** thereby leading to massive fluid shifts. At the same time because of the loss of fluid from the circulation often combined with a degree of dehydration a potent anti-diuretic hormone (ADH) response causes the kidneys to retain water resulting in a low volume concentrated urine, high in sodium. This may be compounded by the administration of a "fluid challenge" to elicit an improved urinary output.

This is a "double whammy" excess free water is administered and excess free water is retained. Water is drawn across blood capillaries into the interstitial and intracellular spaces. The child will become "puffy" looking and of greater consequence the brain will swell with the shift of water, leading to seizures and herniation of the tentorium and death. Therefore to prevent hyponatraemia we must limit the free water component of intravenous fluids AND monitor urine output and serum chemistry.

Recommendations:

1. Regular measurement of blood biochemistry, including a baseline measurement and measurements following each intervention, eg, fluid resuscitation or surgery.

2. Maintenance fluids should be calculated separately from "replacement" fluids. The rate of maintenance fluid is critically dependent on body weight, which should be accurately measured or estimated by a professional with substantial paediatric experience.

3. DO NOT give GLUCOSE containing intravenous fluids for fluid resuscitation. This is in keeping with APLS recommendations (use 0.9% NaCl, Normal Saline or other salt solution). You MUST measure blood sugar and administer a GLUCOSE bolus if there is hypoglycaemia (< 3 mmol/L).

AVOID albumin as an immediate fluid bolus unless there are specific indications. Fresh Frozen Plasma (FFP) is indicated if there are infection or coagulopathy problems.

The usual resuscitation volume is 10-20mls/kg bolus over 15-60 minutes depending on the clinical state.

4. Maintenance fluid should contain at least 0.45%NaCl in 2.5% Glucose. A balanced salt solution such as Normal Saline or Hartmann's does not contain glucose. Regular, 12 hourly, blood sugar estimation is required and must be documented.

CAM

5. Measurement of urine output or body weight is mandatory. Daily body weight measurement will accurately assess free fluid but is not feasible in the surgical bed bound child with acute pain. Urine output must be measured and clearly documented. An experienced doctor must assess fluid balance at least twice daily and take appropriate action to correct fluid loss or retention. If urine output is problematic a urinary sodium, potassium and urea should be measured.

6. Care must be exercised when additional fluids are administered as this may seriously complicate the maintenance fluid regimen. Intravenous antibiotics, oral fluids or contrast media are commonly forgotten additional fluids.

Type of IV fluids	Volumes	Type of solution		
		<10kg and Na=140-145 mmol/L	>10kg and Na=140-145 mmol/L	All weights and Na< 140mmol/L
Maintenance Fluids in 24 hour period	1st 10 kg (0-10) = 4 mls/kg/hr 2nd 10 kg (11-20) =2mls/kg/hr Subsequent kg = 1 ml/kg/hr i.e. for a typical 4 year old of 16kg this would translate to 52mls/hr (40mls+12mls)	0.18 NaCl solution in 4% glucose (if well) 0.45% NaCl solution in 2.5% glucose (if sick or post-op)	0.45% NaCl solution in 2.5% glucose	Ask for advice Usually Normal saline or Hartmann's
Replacement of previous losses	Replace equivalent volume lost ie correction of dehydration over 24-36 hours	Usually Normal saline or Hartmann's		
Ongoing losses	Replace equivalent volume lost at intervals	Depends on type of loss ie gastric losses replaced with Normal saline		

IV Fluid replacement = maintenance + replacement + ongoing losses

10/06/2001

Proposal For Use Of Intravenous Fluids In Children At Craigavon Area Hospital

It is proposed that the following approach includes all children aged over 6 months, including

Perioperative patients

General medical patients (unable to tolerate oral intake)

Accident and Emergency Ressuscitation

It stems from and is driven by the wealth of evidence to support the fact that dextrose containing fluids provide an excessive water load which cannot be cleared in the setting of acute illness (in the broadest sense) due to elevated arginine vasopressin (AVP) levels. It recognises the estimated 10- 15,000 deaths in the UK and Europe due to the consequent hyponatraemia and its neurological sequelae. It is of note tragedies occur to this day often reflecting misguided prescribing based upon out-dated theories and teachings.

A major advance would be if the ONLY fluids to be stocked by the wards and departments caring for children were to be:

0.9% Sodium chloride

Hartmann's solution (Ringer's lactate)

Other "hypotonic" dextrose/saline solutions should be removed to prevent their use e.g. 0.18% and 0.45% saline.
It is accepted hypernatraemia may rarely complicate such a regime on occasions and therefore a limited supply of 5% dextrose should be available to correct the rare cases of documented hyperosmolar hypernatraemia, given in a pre calculated dose to correct the water deficit. This is acting as a "safe" form of intravenous water and for no other purpose. It is also acknowlcged an oral source of water is frequently feasible.

In terms of "volume" we would propose retaining the standard regime below for hourly maintenance:

$4 ml kg^{-1}$ for the first 10 kg
$2 ml kg^{-1}$ for the next 10 kg
$1 ml kg^{-1}$ for subsequent kg's

(For example a typical 4 year old of 16kg would receive 52 $ml hr^{-1}$ of isotonic maintenance fluid).

Replacement of deficits should be directed to expanding the extracellular and circulating volumes and maintaining tissue oxygen delivery- guidelines here are not realistic . Again, only isotonic salt solutions (with colloid if the practitioner prefers) can be justified and must be dictated by clinical need with titration to effect. A plasma urea and electrolyte assay should be taken prior to all intravenous fluid infusions and subsequent electrolyte assays performed at least daily as a minimum. These should be more regular if indicated and certainly repeated in the setting of hyponatraemic symptoms (see below). It is also strongly advocated that plasma osmolality be measured when plasma sodium is less than 140 mmol/l.

It is a point of principle that intravenous fluids are stopped at the earliest opportunity with a return to a balnced oral intake being a priority. It should not be forgotten hypotonic oral fluids are also potentially dangerous in this context- the use of hypoosmolar feeds and fluids in the community is currently the commonest cause of non febrile seizures in the <2 year old population in the US.

Similarly it must be remembered while using isotonic salt solutions reduces risks, hyponatraemia is well recognised due to pathological excretion of hypertonic urine ("desalination" of fluids) and this further reinforces the value of regular assays.

Symptoms of hyponatraemia are generally insidious but typical, with neurological sequelae being especially a risk in children. Early warning is given by:

Headache
Nausea and vomiting
Altered or depressed consciousness.

Failure to recognise these features is typically followed within hours by:

Convulsions/ status epilepticus
Respiratory arrest/ cerebral hypoxia
Coma
Elevated intracranial pressure, coning and death.

Vigilance to this problem is essential if long term sequelae are to be prevented.

Common sense would dictate all intravenous infusions for children include a burette and a drip counter, ideally with some form of anti-syphon valve.

It is to be suggested that urine electrolytes and osmolality provide complimentary information regarding renal dynamics- and furthermore that the excretion of a hypertonic urine is common and not an indication to use a "reduced sodium" fluid.

It is recognised that concerns exist regarding hypoglycaemia during prolonged intravenous fluid infusions. We recognise this and acknowledge hypoglycaemia is dangerous but would point out:

Glucose homeostasis is well developed beyond 6 months and rarely problematic at 1 year

Glucose could be added to 0.9% saline, thus meeting both sodium and glucose requirements
Hartmann's solution with its 29 mmoll lactate content provides an excellent source of glucose (equivalent at least to an infusion of 5 $mmoll^{-1}$ glucose).

NOTES:

Given the relative lack of good quality data on what is likely to be a massive clinical risk/ problem then audit should be an integral part of any revised fluid protocol- at the very least to highlight the risks to the many people unaware of the problem.
Good quality monitoring of sodium and electrolytes would allow validation or revision of this regime in an evidence based way.
It is also to be encouraged that regular urine electrolyte and osmolality assessment would compliment plasma values and elucidate some of the mechanisms behind "illness" hyponatraemia.

The proposed age limit for this protocol is 6 months. Clearly this may be an area for discussion.

A major area will be re-education of medical, surgical and anaesthetic staff in addition to the paediatric nursing staff. Most of the current practise is based on physiological principles from studies performed 40 years ago and while this remains the teaching of most "standard" texts and medical schools, the evidence from practise shows we must "re-learn" our undersatanding of paediatric illness and electrolytes/fluids. In the mean time a strict fluid protocol eliminating effectively hypotonic fluids and selective stocking of fluid will act as a safety factor to reduce poor prescribing.

There is a need for better recording of fluid and electrolyte prescriptions, monitoring and fluid balance in paediatric patients. The recent NCEPOD recommendations highlighted the need for fluids to be approached with the same respect as any other drug given to patients. Good data will further aid audit and improve outcome.

Hartmann's solution carries a number of significant advantages over 0.9% saline as a fluid (including reduced chloride and acid load, and lactate as a source of glucose and proton consumption). In paediatric anaesthesia we have extensive experience of this fluid and would suggest it would transfer to paediatric medical patients very well. We recognise there is a degree of suspicion regarding this unfamiliar fluid but would welcome any suggestions upon its use.

The literature reports 15,00 deaths p.a. in the US due to hyponatraemia, the figure for Europe being approximately 10-15,000. At a regional level (and within Craigavon Area Hospital) the consequences of hyponatraemic fluids in children have been tragically seen. Hyponatraemia tends to kill or leave profound neurological impairment. Children are an especially high risk group. A failure to radically revise and modify our prescribing would quite rightly be seen as poor practise and indefcnsible.

It is to be hoped in the future some consensus within the hospital be reached regarding the optimal treatment of hyponatraemia. While we do not wish to dilute the key message of the above recommendations if hyponatraemia occurs a strategy should be in place regarding its management, given the disastrous consequences.

CAHCTT

Retrospective Chart Audit – Appendicectomy (< 14 yrs)

4/12: 1/4/01 → 30/7/01 11 pts.

Age 3 – 13 yrs. mean 10

6/11 appropriate fluids peri- + post-op. N/S or R/L

2 out of the 6 – 1 prescribed 5/.D/D but cancelled by anes.
1 prescribed No. 18 SOL^n

5 pts: No. 18 SOL^n pre-op (often vomity).

Pre-op U+E: 9/11 Range: 132 – 139. Mean:

No post-op U+E's

Nat 132
135
134
137
No U+E

} Pre-op No. 18 SOL^n

only 1 child received post-op No. 18 SOL^n

DRAFT

Minutes of the Morbidity / Mortality and Audit meeting held on
Friday 14 December 2001 in the Postgraduate Centre, CAH at 8.30 a.m.

Present:

7. **Fluid Balance Charts (pilot project) - Dr H Archbold**

This project was narrowed to establish if the fluid balance charts were fully completed and calculated accurately. None of the five charts piloted met all of the criteria. It was unanimously agreed this project should be carried forward. It was agreed Mr Mackle and Mr Hewitt would liaise with the Sisters to establish how this audit could be further developed on a multi-professional basis.

8. **Date of next meeting**

The next meeting will be held on Friday, 11 January 2002.

Pon

Hyponatraemia in children

Dilutional Hyponatraemia has been documented in otherwise healthy children following routine elective surgery. It occurs in often female children 3-10 years of age and is associated with "stress". Risk factors include; Hypernatraemia, dehydration (>7%), Stress; Nausea, pain, anxiety, certain drugs, disturbances of the Central Nervous System and Metabolic and Endocrine disorders.

A fluid for children recommended for many years as a standard is 0.18 NaCl in 4% Glucose. It contains 30 mmol/l of sodium which when administered at the calculated rate (4 mls/kg/hour for the first 10 kgs body weight) provides the daily requirement of sodium and glucose.

0.18 NaCl in 4% Glucose is **isotonic** *in vitro* ie has the same osmotic potiental so will not cause fluid shifts within the body. However in the catabolic (sick) child the glucose is metabolised rapidly causing the fluid to become ***hypotonic*** thereby leading to massive fluid shifts. At the same time because of the loss of fluid from the circulation often combined with a degree of dehydration a potent anti-diuretic hormone (ADH) response causes the kidneys to retain water resulting in a low volume concentrated urine, high in sodium. This may be compounded by the administration of a "fluid challenge" to elicit an improved urinary output.

This is a "double whammy" excess free water is administered and excess free water is retained. Water is drawn across blood capillarics into the interstitial and intracellular spaces. The child will become "puffy" looking and of greater consequence the brain will swell with the shift of water, leading to seizures and herniation of the tentorium and death. Therefore to prevent hyponatraemia we must limit the free water component of intravenous fluids AND monitor urine output and serum chemistry.

Halberthal M et al studied 23 patients studied with acute hyponatraemia. All received hypotonic fluids (plasma Na+ < 140 mmol/l). 16 (70%) received excessive maintenance fluids (>50%). 13 (57%) were postoperative patients and 18 (78%) developed seizures. 5 (22%) Died (Brainstem death), 1 severe neurological deficit.

pdm

Recommendations to prevent Acute
Hyponatraemia in Children

To prevent the uncommon but serious problem of dilutional hyponatraemia the free water component of intravenous fluids must be limited. Acute hyponatraemia is often unheralded, therefore care must be taken in the prescription and administration of intravenous fluids. Finally surveillance of the patient receiving intravenous fluids is vital.

1. **Body weight** must be accurately measured or estimated by a professional with substantial paediatric experience. The estimation of body weight can be made using the child's age; **Body weight = (AGE+4) x 2**
This weight should be plotted on a Centile Chart as a cross check. If the weight is beyond the 3rd or 97th Centile range then the weight must be re-examined.

2. **Fluid Calculation.** Maintenance fluids should be calculated carefully.
An accepted guide to maintenance fluid administration is;

For the first 10 kgs body wt give 4 mls / kg / hour *(40 mls/hr for a 10 kg infant)*
For the second 10 kgs body wt give 40 + 2 mls / kg / hour *(60 mls/hr for a 20 kg child)*
For each subsequent 1 kg body wt give 60 + 1 ml / kg / hour *(70 mls/hr for a 30 kg child)*

3. **Maintenance fluid** should contain **at least** 0.45%NaCl in 2.5% Glucose.

4. **Chemistry.** A baseline blood sample must be sent for Na+, Urea and blood sugar. Regular Na+ and blood sugar estimation is required and must be documented. This will mean at least once and often twice daily samples. An indwelling heparinised cannula or capillary sample will avoid sampling difficulties in the anxious child or those with poor veins. Do not take samples for the same limb as the intravenous infusion.

5. **Other Fluids.** DO NOT give GLUCOSE containing iv fluids for fluid resuscitation. This is in keeping with APLS recommendations (use 0.9% NaCl, Normal Saline or other salt solution). Give 5 mls/kg 10% GLUCOSE bolus if there is hypoglycaemia (< 4 mmol/L). Care must be exercised when additional fluids are administered. Intravenous antibiotics, oral fluids or contrast media are commonly forgotten additional fluids.

6. **Fluid balance.** Measurement of urine output or body weight is mandatory. Daily body weight measurement will accurately assess free fluid but is not feasible in the surgical bed bound child with acute pain. Urine output must be measured and clearly documented. An experienced doctor must assess fluid balance at least twice daily and take appropriate action to correct fluid loss or retention. If measurement of urine output is problematic a urinary sodium, potassium and urea should be measured.

7. **Correction of hyponatraemia.** A Child with a serum Na+ < 130 mmol/l needs urgent referral to a hospital with a Paediatric ICU (Asymptomatic hyponatraemia). Correction of hyponatraemia is potentially dangerous and requires experience

DOH

Intravenous Fluid Prescription

Infants less than 1 year of age.

Dilutional Hyponatraemia does not appear to be a common problem in this age group. Blood chemistry and monitoring of fluid balance is as described above.

For normal serum sodium (Na+ 135-145 mmol/l)
Give 0.18% NaCl in 4% Glucose at a rate of 4 mls per kg body weight per hour. *Eg For a 5 kg infant this is 20 mls per hour.*

For low or high sodium expert advice should be sought.

Children greater than 1 year of age.

Dilutional Hyponatraemia is well documented in this age group. Blood chemistry and monitoring of fluid balance is as described above.

For normal serum sodium (Na+ 135-145 mmol/l)
Give 0.45% NaCl in 2.5% Glucose at a rate as above.

For low or high sodium expert advice should be sought.

REFERENCES

Arieff AI. Postoperative hyponatraemic encephalopathy following elective surgery in children. Paediatric Anaesthesia 1998:8:1-4

Halberthal M et al, Acute hyponatraemic in children admitted to hospital. BMJ 2001;322:780-2

Paediatric Anaesthesia 1998 8: 1–4

D. Lowry

Editorial
Postoperative hyponatraemic encephalopathy following elective surgery in children

ALLEN I. ARIEFF MD
Department of Medicine, University of California School of Medicine, San Francisco, CA, USA

Introduction

In the United States, there are an estimated 15 000 deaths per year as a consequence of postoperative hyponatraemia (1) (Figure 1). There have been a number of recent studies which have described postoperative hyponatraemic encephalopathy with death or permanent brain damage (2–6). From these studies, it appears that brain damage associated with postoperative hyponatraemic encephalopathy primarily affects menstruant women (1) and prepubertal children (6).

Postoperative hyponatraemic encephalopathy in prepubertal children

There are multiple reports of prepubertal children suffering brain damage from postoperative hyponatraemic encephalopathy (6–9). The aetiology of the hyponatraemia usually involves a combination of: a) intravenous hyponatraemic fluids; b) elevated plasma antidiuretic hormone (ADH); c) respiratory insufficiency secondary to hyponatraemic encephalopathy. It has been demonstrated in several series that plasma levels of ADH (vasopressin, antidiuretic hormone) are elevated in virtually every postoperative child (7,10–13). If such patients are given intravenous free water (any solution with a sodium concentration below 140 $mmol \cdot l^{-1}$), there will always be a tendency towards postoperative hyponatraemia (14). When compared with other groups, prepubertal children are far more susceptible to brain damage from hyponatraemia than are adults (6), and recent experimental evidence demonstrates why this may be the case.

Correspondence to: Allen I. Arieff, 299 South Street, Sausalito, CA 94965, USA.

Effects of hyponatraemia on the paediatric central nervous system

Nattie & Edwards (15) studied the effects of acute hyponatraemia on the brain of puppies. They found that acute lowering of plasma sodium from 140 to 120 $mmol \cdot l^{-1}$ resulted in severe hypoxaemia (arterial PO_2 fell from 11.4–6.9 kPa (88 to 53 mmHg)) and cerebral oedema. In contrast to adults, the brains of paediatric animals (three day old puppies and neonatal rats) were unable to adapt to hypo-osmotic stress by extrusion of cation (15,16).

Adaptation of the brain to hyponatraemia occurs as a consequence of the following sequence of events. First, hyponatraemia leads to a movement of water into brain cells as a result of osmotic forces. In addition, vasopressin which is usually elevated in the plasma of hyponatraemic patients (17) may lead to a direct movement of water into brain cells independent of the effects of hyponatraemia (18). The early response of the brain to this hyponatraemia-mediated oedema is the loss of blood and cerebrospinal fluid, followed by extrusion of sodium from brain cells by several pathways (19). Loss of potassium and possibly organic osmolytes follows later, in an attempt to decrease brain cell osmolality without a gain of water (20).

Effects of hormones and physical factors on brain adaptation to hyponatraemia

There is a significantly higher intracellular brain water content in prepubertal rats in comparison with adult rats, suggesting that the brain occupies a greater percent of the available intracranial volume in young rats (16). Such physical factors may be important determinants of outcome in hyponatraemic rats. As individuals age, there is a progressive decline in the volume of brain, while skull size remains constant in adult life (21). Thus, elderly individuals of both

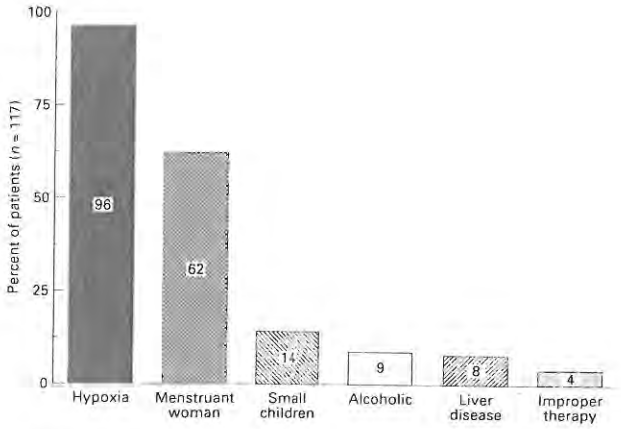

Figure 1
In nine published series from our laboratory comprising 847 hospitalized patients with postoperative hyponatraemia, 19% (158/847) developed hyponatraemic encephalopathy and 117 developed permanent brain damage or died. The major risk factors associated with permanent brain damage in these 117 patients with hyponatraemic encephalopathy are shown. Most patients (96%) suffered an hypoxic episode because of failure to initiate active therapy in a timely manner. In 4% of patients suffering permanent brain damage, improper therapy for hyponatraemia was implicated in the outcome.

genders have more room in the rigid skull for the brain to expand than do younger ones. This finding is more marked in males (21).

If adaptation of the brain is not adequate, pressure of the swollen brain on the rigid skull leads to a decrease in cerebral blood flow (22) and cerebrospinal fluid production (23). If the ability of the brain to adapt is impaired, there will be increasing oedema, with eventual tentorial herniation and secondary cerebral ischaemia (24). This often leads to respiratory insufficiency (4), with reduced delivery of oxygen to brain because of the further decrease of cerebral blood flow, thereby exacerbating the existing cerebral ischaemia (22).

Sex steroid and certain neuropeptide hormones may influence brain adaptation to hyponatraemia. Male rabbits and cats are more efficient than females in extruding sodium to decrease brain cell osmolality during hyponatraemia, resulting in significantly less brain swelling in male than in female hyponatraemic animals (16,25). Oestrogens have also been reported to stimulate, and androgens to suppress, vasopressin release (26,27). Virtually all hyponatraemic patients have increased plasma levels of vasopressin (17,28), a neuropeptide which may exert multiple potentially deleterious cerebral effects. In normonatraemic animals vasopressin results in water accumulation in the brain (18), a significant decline in brain synthesis of ATP (29), and a decline of brain pH (29,30). Vasopressin also impairs the function of several important adaptive pathways to hyponatraemia (31,32).

Recent studies have demonstrated that the brains of prepubertal rats are unable to adapt to hyponatraemia (16). The greater mortality with hyponatraemia in prepubertal rats is associated with a greater accumulation of water in the intracellular space of the brain than in rats belonging to other age groups, as well as an inability of the prepubertal brain to extrude sodium from brain cells. The baseline intracellular sodium content in the prepubertal rats was greater by almost 50% than in control adult rats, a finding consistent with previous studies in newborn dogs (15,33).

Biochemical differences in paediatric vs *adult brain with hyponatraemia*

There are several possible reasons for the increased brain intracellular sodium in prepubertal rats. The Na^+-K^+ ATPase system appears to be the major early adaptive pathway for extrusion of sodium from brain cells during hyponatraemia (19,34) and its impairment results in decreased ability to pump sodium out of the brain. In prepubertal rats, the brain Na^+-K^+ ATPase activity is significantly lower than that observed in adults, both *in vitro* (35) and *in vivo* (36). Coupled with the higher brain sodium, these differences may reflect a limited ability to pump sodium out of the prepubertal brain. The increased intracellular sodium content may be a consequence of limited cerebral Na^+-K^+ ATPase function in young rats compared to adults. The decreased cerebral Na^+-K^+ ATPase activity may be responsible for the impaired adaptation to hyponatraemia in prepubertal rats. Testosterone stimulates Na^+-K^+ ATPase activity in rat brain (37,38). Pretreatment of prepubertal rats with testosterone resulted in a significant decrease in the brain intracellular content of both sodium and water while also reducing the mortality associated with acute hyponatraemia from 84% to zero (16).

Clinical effects of hyponatraemia in children vs *adults*

If one can extrapolate the above experimental findings to paediatric patients, then the implications would be that children are more susceptible to brain damage from postoperative hyponatraemia than are adults. The reasons include: a) decreased available

room for swelling of the paediatric brain in the rigid skull, leading to a propensity for brain herniation with what might appear to be a small decrement of plasma sodium (39); b) impaired ability of the paediatric brain to adapt to hyponatraemia when compared with adults (15,37); c) severe systemic hypoxaemia secondary to respiratory insufficiency frequently occurs in children with only modest hyponatraemia (6,15,39). The respiratory insufficiency is a consequence of increased intracranial pressure (3).

Gomola *et al.* have described a prepubertal (10 years old) female child with middle face hypoplasia who underwent elective maxillary reconstruction (40). The surgery went well and postoperatively, she was given primarily free water intravenously (280 mM glucose in 51 mM NaCl) at a rate of 2 l per day. The child weighed 30 kg with estimated total body water of 18.5 l. On the first postoperative day, the child became confused and developed headache and vomiting. Renal function was apparently normal on the basis of normal plasma urea and creatinine. The plasma sodium was found to be 117 $mmol \cdot l^{-1}$. She was initially treated with sodium supplementation, but on the second post-operative day, the plasma sodium was still low at 120 $mmol \cdot l^{-1}$. The urine and plasma osmolalities were 342 and 255 $mOsm \cdot kg^{-1}$. An MRI of the brain was normal. The authors proposed three possible explanations for the hyponatraemia: a) dilutional hyponatraemia secondary to IV hypotonic fluid; b) pituitary insufficiency; c) inappropriate secretion of ADH. Pituitary insufficiency was ruled out by normal values for ACTH, cortisol, thyroid hormone and growth hormone. The ADH was 4 to 5 $pg \cdot ml^{-1}$, which is 'normal' but inappropriately high for the extracellular hypoosmolality (41) and is essentially a universal finding in both paediatric and adult postoperative patients (7–13). The child received 2 l per day of hypotonic IV fluid in the presence of elevated plasma ADH. Although neither initial plasma sodium, urine output or total volume of IV fluids are provided, given the child's weight and rate of infusion, the plasma sodium of 117 $mmol \cdot l^{-1}$ appears very likely to have been the consequence of retention of about 3 l of IV hypotonic fluid over two days (6). The expression inappropriate secretion of ADS (SIADH) was originally used for elevated plasma ADH related to lung cancer (42) and has become a catch all term for virtually any patient with elevated plasma ADH. In particular, postoperative patients as well as those with heart failure or hepatic cirrhosis have elevated plasma ADH levels but are functionally hypovolaemic as well (41). Postoperative subjects are functionally hypovolaemic, so that the term SIADH may not be appropriate in this patient (11). There is also a perception that ADH, and by association SIADH, can somehow lower the plasma sodium. Although ADH leads to increased retention of ingested or infused water, in the absence of increased water intake, ADH by itself will have no effect upon the plasma sodium. Thus, the most likely explanation for the hyponatraemia in this patient is infusion of hypotonic fluid (51 mM NaCl/280 mM glucose) in the presence of the expected postoperative increase in plasma ADH. Adrenal insufficiency is ruled out by the normal plasma cortisol and the fact that she remained normal for six months without any steroid replacement therapy. Exactly why the plasma sodium rose following IV hydrocortisone is uncertain, but may have been related to the expected decline of ADH values to normal after four to five postoperative days. Pituitary insufficiency is ruled out by normal values for ACTH, IGF1 and growth hormone.

Symptomatic postoperative hyponatraemia carries a mortality of at least 15% (43), particularly in children and respiratory arrest is a frequent occurrence, but once this complication occurs, the morbidity is substantial (6,7). There is no obvious rationale for the administration of hypotonic fluid to a postoperative patient, unless the individual is hypernatraemic (14). If the patient becomes symptomatic, therapy with hypertonic NaCl is indicated (39). The syndrome can be prevented by administration of primarily isotonic fluids to postoperative patients.

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