Witness Statement Ref. No. 008/3

NAME OF CHILD: Adam Strain

Name:Robert Taylor

Title: Dr

Present position and institution: Consultant Anaesthetist, Belfast HSC Trust

Previous position and institution: Consultant Anaesthetist, Belfast HSC Trust
[Since your Witness Statement of 16th May 2011]

Membership of Advisory Panels and Committees:
[Identify by date and title all of those since your Witness Statement of 16th May 2011]
No new membership since 16th May 2011

Previous Statements, Depositions and Reports:
[Identify by date and title all those since your Witness Statement of 16th May 2011]
No new statements since 16th May 2011

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

Ref:	Date:	
011-002	30.11.1995	Draft Statement
011-014	21.06.1996	Deposition of Witness
008/1	18.07.2005	Inquiry Witness Statement
093-038	17.10.2006	Transcript of PSNI interviews
008/2	16.05.2011	Second Inquiry Witness Statement

IMPORTANT INSTRUCTIONS FOR ANSWERING:
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 such a number then please provide a copy of the document.

I QUERIES ARISING OUT OF YOUR SUPPLEMENTAL WITNESS STATEMENT

With reference to your witness statement dated 16th May 2011, please provide clarification and/or further information in respect of the following:

(1) Answer to Question 4(a) at p.3:

"[Adam having retained his native kidneys] meant that he would continue to pass large quantities of urine during a fasting period and throughout surgery. This would obviously have impacted on his fluid management and made the calculations more complex."

(a) Explain the reasons why you did not monitor and measure Adam's urine output from his native kidneys by catheterisation as soon as Adam was anaesthetised.

There is no record of the reason why his bladder was not catheterised. It may have been to permit the bladder to be as full as possible in relation to the operation.

(2) Answer to Question 4(b) at p. 3:

"...The process was managed as I have referred to..."

(a) You have not adequately answered the question. State how the gathering of *"the relevant information"* was to be managed so that there could be a start at 0600. For the avoidance of doubt, if you consider that question has been answered in any of your previous statements please provide the exact reference in that/those statement/s.

Deposition (011-014-096) lines 7-11
Witness Statement 008/1 page 2 Question 1(i) para 1, lines 1-6, para 2, lines 1-5
Police interview (093-038-124) lines 4-13 referring to 058-002-002.

(3) Answer to Question 5(b) at p.3:

"My many questions [that I put to Prof Savage] are not remembered now but the information obtained is referred to in my Coroner's Deposition dated 21.06.96, my Inquiry Witness Statement 008/1, and my police interview of 17.10.96"

(a) State whether you discussed the details of Adam's renal pathology with Professor Savage prior to surgery. If not, explain why.

I would have been informed by Prof. Savage that Adam had polyuric renal failure as the result of congenital posterior urethral valves (011-014-096)

(b) State whether the nature of Adam's renal pathology had any effect on the level and frequency of your attention to the details of Adam's fluid and electrolyte replacement required. If so, state the reasons why, and describe the nature and extent of that effect. If

not, state the reasons why it did not have an effect.

It meant that I had to ensure that sufficient fluids were administered and that any deficits were corrected.

(c) Explain what you understood from your discussion with Professor Savage about Adam's polyuric condition and its implications for your fluid management in relation to the transplant surgery.

I understood that Adam was unable to concentrate urine and that he had large volume dilute urine. The implication was that I would have to ensure that the urine losses were included in the overall fluid calculation.

(4) Answer to Question 5(e) at p. 4:

"I had not seen the notes so could not judge in advance what I would find relevant in them."

(a) You have not adequately answered the question. Please describe and explain what information you would be seeking in Adam's medical notes and records and *"the relevance of it to your plans for Adam's fluid management."*

The question related to the time of the telephone call when I was at home. It was only when I arrived in the hospital that I had the opportunity to read the medical notes.

(5) Answer to Question 5(f) at p.4:

"I can recall going through his notes, reading his current admission including blood investigations, previous anaesthetic records and drug kardex. These were located on the ward as I remember."

(a) State if you saw the document at Ref: 057-007-008 before the operation. If so, state what you considered to be the entry for sodium on this document.

No, it had not been filled in before the operation.

(b) State whether you sought information before Adam was transferred to the operating theatre on:

(i) Adam's fluid balance whilst being dialysed
(ii) the peritoneal dialysis cycles on 26th/27th November 1995
(iii)the volume of urine produced
(iv) the details of all fluid administered to and taken in by Adam
(v) Adam's weight before and after dialysis and how they compared to his normal 'dry weight'
(vi) The time at which Adam last passed urine

I had assumed that his dialysis had been the same as previous occasions. I did not receive any information that it had been otherwise.

(c) If you did state when you did so, from whom and state the response that you received. If you did not, explain the reason why.

(d) If you were given that information, state when and by whom. Identify where this information is recorded. If you were not given this information, state the reasons why not.

(6) **Answer to Question 6(a) at p.4:**

"I meant [by the usual maintenance rate] the rate that Dr. Savage would consider appropriate."

(a) State *"the rate"* which you think Adam should have received.

I deferred this decision to Dr Savage.

(7) **Answer to Question 6(b) at p.4:**

"The type and volume of IV fluids [prescribed to be administered] were those which Dr. Savage considered appropriate."

(a) State *"the type and volume of IV fluids"* which you think Adam should have received.

I deferred this decision to Dr Savage.

(8) **Answer to Question 6(c) at p.4:**

"A check on Adam's U&E pre-operatively would be routine in a patient undergoing peritoneal dialysis prior to kidney transplant."

(a) State the extent of your experience by 26th/ 27th November 1995 of anaesthetising patients regularly undergoing peritoneal dialysis and relate this to your claim that *"a check on Adam's U&E pre-operatively would be routine"*.

I have no records of the numbers of patients regularly undergoing dialysis prior to these dates. It was usual for a pre and post-dialysis U&E to be available before an anaesthetic.

(9) **Answer to Question 7(a) at p.4:**

"I am aware from Dr. Montague's police statement (093-037-113) that he reports advising me by telephone during the night regarding Adam's iv access however I do not recollect that telephone call now. I had previously believed it was shortly after I had arrived on the ward that I first learned of the problem with Adam's venous access."

(a) State whether you accept that Dr. Montague telephoned you as he describes in his PSNI statement (Ref: 093-037-113).

Yes I accept that he called me as described.

(10) **Answer to Question 7(f) at p.5:**

"I cannot remember the circumstances which led to a change in plan for surgery from 6.00am to 7.00am however my police statement (093-038-125) relates this as a team decision."

(a) Identify the team members who participated in this *"team decision"*.

It would have been the nurses and surgeons as well as myself.

(11) **Answer to Question 8(a) at p.5:**

"The meeting with Adam [at about 05.45hrs] was to assess him pre-operatively. The meeting with his mother was to explain the anaesthetic for the surgery."

(a) State what you did in relation to assessing Adam pre-operatively.

I cannot remember my assessment of Adam preoperatively and it is not recorded. Myself or the anaesthetic trainee would have taken a history, examined the patient and examined his medical records before an anaesthetic.

(b) State whether you clinically examined Adam before administering the anaesthetic, and if so, state when, and what your findings were at that time. Also identify where this examination is recorded. If you did not examine Adam, explain the reasons why not.

I cannot remember my examination of Adam preoperatively and it is not recorded. Myself or the anaesthetic trainee would have examined the patient before an anaesthetic.

(c) State what you said *"to explain the anaesthetic for the surgery"* to Ms. Slavin, and identify all other persons present at this *"meeting with [Adam's] mother"*.

I cannot remember my discussion with Adams mother. My routine is to describe the type of anaesthetic and the procedures that are to be used.

(d) State what anaesthetic risks were explained to Adam's mother and the reasons why. If no anaesthetic risks were explained, state the reasons why not.

I cannot remember my discussion with Adams mother. My routine is to discuss the risks and benefits of the anaesthetic and procedures.

(12) Answer to Question 8(d) at p.5:

"My police statement of 17.10.06 at 093-038-124 reports what was discussed [with Dr Montague about "the effect of having no post-dialysis, U&E results and the impact of no intravenous fluids for the fasting period of the two hours since his night feeds were stopped]."

(a) Your PSNI statement of 17th October 2006 at Ref: 093-038-124 simply repeats what you said in your initial witness statement of 18th July 2005. You have therefore not adequately answered the question. Please describe what you discussed with Dr Montague about *"the effect of having no post-dialysis, U&E results and the impact of no intravenous fluids for the fasting period of the two hours since his night feeds were stopped."*

I have no record of my discussion with Dr. Montague however my Witness Statement WS-008/1 at page 2 second paragraph after the sentence you refer to "I now discussed...with Dr. Montague."goes on to describe what was discussed.

(13) Answer to Question 9(a) at p. 6:

(a) You have not adequately answered the question. Please state the total volume of fluid and content of fluid you concluded Adam had received at the stage of your review of his fluid balance sheet.

He had received a total of 18 mls of 0.18NaCl/4%Glucose iv and 952mls of dioralyte. Total 970mls

(14) Answer to Question 9(b) at p.6:

"The fluid balance sheet (057-010-013) shows a running total of 18 mls of iv fluid (No18) and 952mls of clear fluid (dioralyte) from 2300 to 5.00am. Therefore a total of 970 mls had been given over 6 hours. I calculated that he should have received 1200mls over these 6 hours and therefore he now had to receive in excess of 200ml/hr to provide for this planned fluid administration."

(a) You have not adequately answered the question. Please explain the basis upon which you

say that Adam had received fluids at a rate *"in excess of this 200 ml/hr"* with reference to the fluid balance sheet (Ref: 057-010-013).

I had calculated that he had actually received less (970mls) than had been intended on his fluid balance sheet and would need to receive in excess of 200 ml/hr to correct this.

(b) Specify the rate of administration which you say Adam had received and identify where this rate of administration is documented.

The fluid balance sheet (057-010-013) gives the times and volumes of fluid Adam had received but the rate given requires deduction from these figures.

(c) Explain what you meant by *"now"* when you stated *"I calculated that he should have received ...and therefore he now had to receive...."*

Now meant by the time he arrived in theatre.

(d) State whether you think that, at 05:00, Adam had a fluid deficit, and if so, state what it was.

He had a deficit at 5am. He was meant to receive 200mls/hr from 2300-0500 (6hrs) 1200 mls but had only received 970mls.

(e) State whether you think that, at 07:00, Adam had a fluid deficit, and if so, state what it was.

He had a further deficit of 400 mls by 0700 because of his 2hr fasting period.

(f) For both times, please explain your reasoning in detail, incorporating what your assumptions were regarding Adam's insensible losses, dialysis losses or gains, and urine output.

I had known about his large volume of dilute urine and insensible loss and that during dialysis he did not have net fluid gain or loss.

(g) Explain the effect the peritoneal dialysis Adam received would have had on his hydration status at (i) 0500 and (ii) 0700.

I had known that during dialysis he did not have net fluid gain or loss. This meant that his fluid intake was matched by urine and insensible losses. This would have been the same at 05.00 and 07.00

(15) Answer to Question 9(c) at p.6:

"He had needed to receive the excess between 1.30 and 05.00 (3.5hrs)."

(a) State the period over which you say Adam was administered fluid at a rate in excess of 200 ml/hr and identify the document where this is recorded.

I calculated that by the start of the operation he needed to receive fluid in excess of 200 ml/hr to make up for his deficit and hourly maintenance fluids.

(16) Answer to Question 9(d) at p.6:

"I meant [by saying that Adam was capable of tolerating rates of fluid in excess of normal amounts] he could be given in excess of 200ml/hr because he passed large volumes of dilute urine."

(a) State whether you think there was any limit (in terms of ml/hr) to Adam's urine output. If so, please state what that limit was and explain your reasoning. If not, again explain your reasoning.

I was not certain of Adams upper limit of urine output but was aware that he was not able to

concentrate his urine.

(b) Explain whether you think that if you had given Adam, for example, 2000 ml of IV fluid in one hour, his urine output would have increased accordingly and kept his hydration status normal.

I do not think that he could have coped with 2000 ml of iv fluid in 1 hour. I am not certain if his native kidneys could have coped with this volume of fluid.

(c) State whether you considered it was not possible to give Adam too much fluid during surgery and if so, why. If not, explain why not.

I did not think that I considered that it was not possible to give Adam too much fluid during surgery. I administered the volume and type of fluid that I had calculated to replace his deficit, losses and increase his circulating blood volume prior to a kidney transplant. In addition this fluid was administered by continuous monitoring of his heart rate, blood pressure and observation of the operation site as well as measured and estimated losses.

(d) State whether you think there would be any difference in Adam's hydration status after giving 200 ml/h intravenously for 6 hours compared to giving the same volume at the same rate for the same duration into Adam's gastrostomy (excluding the likelihood of vomiting). If so, please state what that difference would be (excluding the likelihood of any vomiting) and explain your reasoning. If not, again, please explain your reasoning.

I do not think there would be a difference in his hydration between the two methods of fluid administration as for the said exclusions.

(17) **Answer to Question 10(a) at p.6:**

"[The one occasion when Adam had a sodium of 124 mmol/L was] Date 08/06/1995 (058-041-197)"

(a) State if you considered Adam's sodium results prior to June 1995. If so, describe the effect this had on your assessment of Adam's fluid management for his transplant surgery. If you did not consider these results, state why not.

I did consider his previous sodium results. I saw that they were generally stable. The effect on my assessment was to give me confidence that his sodium would remain stable.

(b) In light of Adam's history of occasional hyponatraemia prior to 26 November 1995, state your view on 26th and 27th November 1995 of:

(i) the attention required to be given to Adam's sodium input and actual sodium losses on 26th and 27th November 1995,

(ii) the frequency with which Adam's serum sodium concentration was required to be measured:

- **on admission on 26th November and before and after dialysis and**
- **prior to the commencement of transplant surgery *"knife to skin"***
- **after the commencement of transplant surgery *"knife to skin"* and transfer to PICU**

Ideally a sodium level should have been sent at the commencement of surgery but because of my prioritising of his monitoring and administration of his anaesthetic I did not measure his sodium level accurately until the end of surgery.

(18) **Answer to Question 10(b) at p.7:**

"I could see [that it was usual for Adam's electrolytes to remain stable following dialysis for 24hrs] from his U&E results eg, (058-041-199, 058-041-200, 058-041-201) with only one exception (058-041-197)"

(a) You have not adequately answered the question. Please identify the person who gave you the information that *"it was usual for Adam's electrolytes to remain stable following dialysis for 24hrs"*. Please also state when you received that information.

This information was obtained from my examination of his records not from another person.

(19) **Answer to Question 11(a) at p.7:**

"I could see [information on Adam's previous anaesthetic management] from an examination of his notes. (058-025-069 to 074)"

(a) You have not adequately answered the question. Please state whether or not you sought information about *"Adam's previous anaesthetic management"* from any person or persons, and if so identify that person or persons and describe the information you received from them.

I was referring to his previous anaesthetic records not from another person.

(20) **Answer to Question 12(b) at p.8:**

"The long "cold ischaemic time" meant I did not wish to delay transplanting the kidney by getting iv access or performing blood tests eg U&E."

(a) State how long it would have taken you to take a blood sample from Adam immediately after inducing anaesthesia.

It would have taken one or two minutes.

(b) Explain the reasons why you or Dr Montague did not take a sample of blood from the venous cannula once Adam was safely anaesthetised.

Taking the blood sample also required a form to be filled in and a porter called and the biochemistry department contacted. As stated previously my priority at that time was to monitor and care for Adam and continue his anaesthetic management.

(21) **Answer to Question 13(a) at p. 8:**

"I would have discussed the case with the nursing Sister on duty in PICU, the nursing Sister on duty in theatre and the nurse in charge of the nephrology ward."

(a) In relation to each of those nurses, explain what you were discussing in respect of Adam's case and the reasons why.

I have no record of this discussion. It would have been before the time when Adam arrived in theatre and I commenced his anaesthetic.

(22) **Answer to Question 15(a) at p.8:**

"I knew that he normally received around 150ml/hr input overnight which I would have expected to be matched with similar losses. His urine output is stated as "PU++?how much ?1-2

litres" (058-035-143)"

(a) State whether you considered the Investigation Summary Sheet at Ref: 050-018-055 when you made fluid calculations for Adam's transplant surgery.

Yes

(b) Explain the basis of your expectation that Adam's fluid intake of *"around 150ml/hr input overnight"* would *"be matched with similar losses."*

Because he had polyuric renal failure so I would have expected his urine losses to match his fluid intake.

(23) Answer to Question 15(b) at p. 9:

"We had to provide a similar type and volume of fluids in the background as well as replacing the deficit."

(a) State what you mean by *"in the background"*.

Background means Maintenance fluids.

(24) Answer to Question 15(c) at p.9:

"I was concerned that he was behind in this fluid and we should replace [the deficit] urgently."

(a) You have not adequately answered the question. Please explain the reasons why the alleged deficit needed to be replaced *"urgently"*.

It was to ensure that he had no deficit before I commenced the process of increasing his circulating blood volume so that when the new kidney was attached it would get sufficient perfusion.

(25) Answer to Question 16(b) at p.9:

"Dr Montague was the anaesthetic trainee available at the start of the case as he was also on call with me on that weekend. He was an experienced senior registrar in anaesthesia. He had worked in adult and paediatric anaesthesia and was a good trainee to assist me. He was able to place the epidural and monitor the patient as I was inserting the central line."

(a) State the experience of Dr. Montague in *"paediatric anaesthesia"* prior to 27th November 1995.

He was competent in many of the procedures in paediatric anaesthesia, inserting endo-tracheal tubes, intravenous lines and epidurals. I do not have details of his experience in paediatric anaesthesia.

(26) Answer to Question 17(b) at p.10:

"As in answer 17 (a) It is likely that Dr Montague or the other trainee who replaced him left theatre for a number of minutes for a beverage or a toilet break but I would have remained in theatre during his absence."

(a) State the job title and experience in paediatric anaesthesia of *"the other trainee"* who you state replaced Dr. Montague, and in particular if they were a Senior Registrar.

I cannot remember who it was.

(b) State whether you distinguish between the paediatric anaesthetic experience of Dr. Montague and the incoming trainee. If so, how. If not, state the reasons why not.

I cannot distinguish between the two trainees as I cannot remember who it was.

(27) **Answer to Question 17(d) at p.10:**

"After the start of the surgery another trainee whose name I cannot remember came on duty to assist me and I was able to let Dr Montague go home as he had been on call for 24hrs as he confirms in his statement. (093-037-114). He states that the surgery had just commenced."

(a) State the time at which the other trainee came into your theatre on 27th November 1995.

I cannot remember when this was. I accept Dr Montague's statement that he went home around the expected changeover time of 9am. I would not have allowed him to leave unless an appropriate substitute replaced him.

(b) Describe and explain the arrangements made by *"another trainee ... came on duty to assist [you]"*, including when those arrangements were made and who made them.

I have no record of these arrangements. The replacement trainee anaesthetist will have been the one previously allocated to that theatre session.

(c) State whether there was a handover between Dr. Montague and the other trainee, and if so, state when and where that occurred.

I have no record of the handover.

(d) If there was no handover by Dr. Montague to the other trainee, state:
(i) what information was given or made available to the trainee in relation to Adam and/or the transplant surgery
(ii) how and when that information was provided

I have no information regarding this. I would have told the junior what was happening and what was being monitored during the operation.

(28) **Answer to Question 18(a) at p.10:**

"[An agreed management plan] was [made] after confirming everybody was ready to start."

(a) You have not adequately answered the question. Please explain the particular aspect(s) of the agreed management plan which took a considerable amount of time to work out.

This plan was in relation to administering his anaesthetic and inserting endo-tracheal tube and the venous line, arterial line, CVP line and epidural as well as administering iv fluids to replace his deficit and increase his circulating blood volume prior to the kidney transplant. This plan included ensuring all the equipment was available and ready to use and allocating which of these procedures would be done by Dr Montague or myself.

(29) **Answer to Question 19(a) at p.10:**

"[The reassessment of IV fluids during the first hour] was on a continual basis. We were always aware of the fluids given and lost."

(a) Explain exactly how you were aware of the fluids lost in circumstances where Adam's urine output was not being measured.

I believed that he would continue to lose large volumes of dilute urine as his native kidneys were unable to concentrate urine.

(b) **Explain why IV fluids were reassessed *'several times during the first hour'*, given that surgery had not started and that there were no blood losses.**

Induction of anaesthesia can be associated with a change in his heart rate and blood pressure. The anaesthetic agents and fluid administration need to be watched closely and adjusted as necessary to maintain stability.

(30) **Answer to Question 19(b) at p.10:**

"During anaesthesia we were continually monitoring his vital signs and reassessing his fluids on this continuing basis. Dr Montague and I were involved."

(a) **Specify the *"vital signs"* to which you refer.**

The oxygen saturation, heart rate, blood pressure and end-tidal carbon dioxide levels.

(b) **In relation to how Dr. Montague was *"involved"*, state exactly what Dr. Montague was doing by way of *"continually monitoring [Adam's] vital signs"* and *"reassessing his fluids on this continuing basis"*.**

As in 29 (b) Dr Montague was involved with keeping the patient's respiratory and cardiovascular state stable by adjusting the anaesthetic agent and/or fluid administration in tandem with myself.

(31) **Answer to Question 20(a) at p.11:**

"[State what fluids were in the suction bottle and what fluids were on the towels] Blood"

(a) **Explain how often the swabs were counted and weighed during Adam's surgery.**

Swabs were weighed every-time the scrub-nurse passed them to the circulating nurse (runner).

(b) **Explain the basis of your statement that: *"It was becoming clear that about 200mls of blood was lost in the swabs in the first hour plus a similar amount in the suction bottle and on the towels"* (WS 008/1, p.5, 1st para) given that you also state *"No time-line was present on the swab count form (058-007-020,021) nor was there a time-line of blood volume lost in the suction or spilled on to towels"* (WS 008/1, p.5, 1st para).**

Blood is lost at various stages during an operation. The nurse weighs each swab and writes it on a board that everybody in theatre can see. My administration of fluid is related to the on-going weight (volume) of blood that has been measured in this way.

(c) **If *"during the second hour ie 08.00-09.00 of surgery the blood loss from Adam's swab count (058-007-020,021) became the crucial factor in relation to his fluid management"* (WS 008/1, p.4, final para), explain why *"no time-line was present on the swab count form"* (WS 008/1, p.5, 1st para).**

It was standard practice to record the weight of swabs without a time-line. However, the rate of fluid administration will be in response to the loss of blood at the time it is measured as well as observing changes in Adams heart rate, blood pressure and wound site.

(d) **Please confirm:**

(i) **The time when the induction of anaesthesia commenced**
(ii) **The time when knife to skin occurred.**

From the electronic print-out monitoring commenced at 07.00 which would also correspond to the induction of anaesthesia. There is no record of when knife to skin occurred.

Please provide contemporaneous references for these assertions.
Electronic print-out *(058-008-023)*

(32) Answer to Question 20(b) at p.11:

"Dr Montague or his replacement trainee and I were concerned [about the blood loss]"

(a) State all communication which took place between you and Mr. Keane / Mr. Brown in relation to the impending or actual bleeding during the surgery and the times or stages of surgery at which this was communicated, and what action was taken as a result of this communication

I cannot recall what was said.

(33) Answer to Question 21(a) at p.11:

"[The urine lost by Adam's native kidneys] could not be measured at this stage of the procedure as he was not catheterised. When he had his suprapubic catheter inserted at the end of the procedure we could measure his urine volume".

(a) Please explain why a urinary catheter was not inserted soon after anaesthesia was induced.

As in Answer 1a. This was to permit the bladder to be as full as possible in relation to the operation.

(b) State whether there was any contra-indication to inserting a urinary catheter immediately after induction of anaesthesia, and if so, identify it.

Yes, it would have resulted in an empty bladder.

(c) State whether it was your decision not to insert a urethral catheter before commencement of surgery. If it was not your decision, state whose decision it was. State whether, in retrospect, you think it was the correct decision. Please explain your reasoning in both cases.

I expect it was a result of discussion with the surgeons although I cannot remember. A catheter would have provided me with information on urine output and the surgeon with an empty bladder. Without it there is no information on urine output but the surgeon has a full bladder.

(34) Answer to Question 22(b) at p.11:

"[The basis upon which I was reasonably satisfied that the renal losses were now adequately replaced] was based on the calculations of his deficit and requirements. We had given 1000mls of 0.18NaCl/4%Glucose and 400mls of HPPF giving a total input of 1400mls and a loss exceeding 500mls of blood and urine lost by Adams native kidneys"

(a) State what you assumed to be the volume of *"urine lost by Adam's native kidneys"* during the procedure <u>prior</u> to the puncturing of his bladder and/or insertion of suprapubic catheter. Please explain your reasoning.

I did not know what his urine volume was during the procedure. I knew that he was passing large volume dilute urine that I estimated to be 200 ml/hr.

(35) Answer to Question 24(e) at p.12:

"After I concluded that the CVP line was "obstructed" in the neck the CVP could not be trusted as an absolute number but could be useful as a relative marker."

(a) State the CVP reading you expected to find in Adam when the CVP catheter was first placed (taking into account the fluid volume you had been infusing during the time 0700-0800) Please explain in detail your reasoning.

I expected his CVP to be 8-10 mmHg as I had been administering fluid to replace his deficit and he was losing dilute urine.

(b) State how much you intended to increase the CVP above that expected pressure and explain your reasons.

I intended to increase it by 4-5 mmHg above the normovolaemic level but the actual level varies in relation to other measurements, HR, BP and the performance of the kidney.

(c) Explain what the implications for your fluid management would have been had the CVP readings you obtained been accurate.

I would have aimed to ensure that Adam was hydrated and normovolaemic and then increased the fluids to increase his circulating blood volume prior to the kidney transplant.

(d) State if you examined the dynamic trace of the CVP. If you did so, describe the waveform of the dynamic trace. If you did not, explain why not.

I did examine the dynamic trace and it was non-pulsatile which confirmed my clinical findings that the tip had gone into the neck.

(e) State whether you informed Mr. Keane / Mr. Brown / Professor Savage / Dr O'Connor during the transplant procedure of:
(i) any difficulties with the central venous line insertion
(ii) your view of the CVP readings,
and if so, state exactly what information was given, to whom and when was it given.

I have no recollection of my conversation with the doctors mentioned but it is my usual practice to inform them if I was having difficulty with CVP access and accuracy.

(f) If you did not give this information to Mr. Keane / Mr. Brown / Professor Savage / Dr O'Connor during the transplant procedure, state the reasons why not.

N/A

(g) Once you concluded that *"the CVP line was 'obstructed' in the neck"*, state what consideration, if any, you gave, to an alternative strategy e.g. withdrawing the tip of the CVP line slightly, reinserting the CVP line, surgical cutdown, etc. If you did consider an alternative strategy, state your reasons why. If you did not, state the reasons why not.

I had attempted to withdraw and re-wire the line and re-insert it but I was still able to palpate it in his neck. I considered trying his other subclavian but I was not certain that I would have been successful in locating the vein or that it would have found its way into a better position in his SVC. Also further attempts would have further delayed surgery.

(h) Once you *"concluded that the CVP line was 'obstructed' in the neck [and] the CVP could not be trusted as an absolute number"*, state the reasons why you concluded that the CVP could be trusted to *"be useful as a relative marker."*

The reading was higher than expected because it was obstructed. However it was still in a central vein and changes in his circulating blood volume would be reflected in changes to this pressure. Thus a relative increase in his circulating blood volume would lead to an increase in the CVP relative to the initial level.

(i) **Explain what effect the obstruction of the CVP line in the neck could have on the reliability and validity of the CVP measurement *"as a relative marker."***

Although I knew that the tip was in a central vein and changes in Adams circulating blood volume should increase his CVP reading I was not confident that it was very reliable and therefore took other measurements (HR, BP) into consideration when deciding if he was hypervolaemic.

(j) **State whether it would have been possible to carry out *"a pre-operative x-ray"* on 27th November 1995 *"to check line position"* in relation to the CVP. If it was possible, state why you did not do this. If not, state why not. State whose responsibility it would have been to obtain such an X-ray.**

It would have been possible to do a pre-operative X-Ray but I did not do this as I had determined that the tip of the CVP had gone up into the neck by palpating it there.

(k) **State where you consider the CVP line ended in light of Adam's x-ray (Ref: INQ-0340-11) and state what effect that positioning would have had on the CVP readings during surgery, and in particular, whether it would have decreased or increased the CVP**

The Xray confirmed my assessment that the tip had gone up into the neck. Positioning of his head could have obstructed the tip still further by "kinking" the neck vein. I had tried to prevent his kinking by keeping his head and neck as straight as possible.

(36) **Answer to Question 25(a) at p.13:**

"Blood loss as recorded on the blood loss form (058-007-021), Blood pressure as recorded on the anaesthetic record form (058-003-005), CVP as recorded on the CVP trace (058-008-023) and general status-other parameters on the anesthetic (sic) record form (058-003-005), all were indicators that further fluid may potentially be required."

(a) **You have not adequately answered the question. Please state the particular aspects of the *'blood loss'*, *'blood pressure'*, *'CVP'* and *'general status'* which indicated to you that *"further fluid may potentially be required"*.**

Blood loss was measured throughout the procedure by weighing the swabs and looking at the suction level and towels. Blood pressure will be affected by the amount of blood in the circulation so I inserted an arterial line at the start of the anaesthetic to keep a very close watch on his blood pressure/blood volume. CVP is a measure of the amount of circulating blood in the venous side of the circulation. Keeping close observation on these aspects as they relate to each other is what I meant by his general status.

(37) **Answer to Question 25(b) at p. 13:**

"When observed blood loss exceeded 400mls corresponding to 25% of Adam's blood volume there was a need to consider giving blood."

(a) **State the stage of surgery and time at which *"observed blood loss exceeded 400mls"*.**

09.32, this corresponded to my measurement of his haematocrit which confirmed that he required the administration of blood.

(b) **State how you knew that this blood loss had occurred at that stage of surgery or at that time.**

From the swabs, suction bottle and observed loss in the towels.

(38) **Answer to Question 26(a) at p.13:**

"It could have been me, the trainee anaesthetist or the medical technical officer on duty."

(a) State the location of the blood gas machine on 27 November 1995 to which you could have transported the blood sample for testing, and the proximity of that machine to the operating theatre where Adam's renal transplant was taking place.

In the PICU about 20 yards from the theatre as marked on the site plan previously supplied to the Inquiry

(b) State if it would have been possible for Dr Savage to take the blood sample to the blood gas machine for analysis. If not, explain why not.

Dr. Savage could have taken a sample to the analyser but he was not trained in its use and he wasn't in theatre when the sample was taken.

(c) If Dr Montague, the other 'trainee anaesthetist' or the Medical Technical Officer were not trained to use the blood gas machine, state whether arrangements could have been made to give a sample to one of the ICU staff for them to perform the analysis.

The MTO, Dr. Montague and the other trainee would have been trained in the use of the analyser.

(39) **Answer to Question 27(a) at p.13:**

"The sodium content of the sample is likely to have been altered by the addition of heparin to the sample syringe."

(a) Explain how *"the addition of heparin to the sample syringe"* is likely to alter the sodium concentration result.

It alters the dilution of the blood sample.

(b) Explain whether *"the addition of heparin to the sample syringe"* was likely to raise or lower the sodium concentration result and to what extent.

It would lower the sodium level by an indeterminate amount.

(c) State the type of heparin solution used to anticoagulate blood in the syringes used in blood gas machines in the RBHSC in November 1995.

I do not have a record of the heparin used in November 1995

(d) State whether heparin was added to the sample syringe, and if so, state by whom and the amount of heparin added.

It was vital to add heparin to the blood gas sample to prevent clotting inside the machine. I did not record who added the heparin or the volume of heparin added.

(40) **Answer to Question 27(b) at p.13:**

"The factor that led me to check blood loss was the Haematocrit of 18, normally around 30."

(a) Explain how often during the course of surgery, particularly one with significant blood loss, you would normally check the haematocrit level by using a blood gas machine.

I would perform a haematocrit test if and when the blood loss reached about 20% of the circulating blood volume.

(b) **Explain the reasons why during surgery, given the amount of blood loss, the first blood gas analysis was carried out at 0932, rather than earlier.**

It was not performed earlier as the blood loss had not reached 20% of the circulating blood volume.

(c) **State the times at which any further blood gas analysis was carried out during the transplant procedure.**

There was no further blood gas analysis during the procedure.

(41) Answer to Question 27(c) at p.14:

"It was not the low sodium which resulted in the re-appraisal of blood loss, see 27b"

(a) **Describe and explain your response/reaction, if any, to the *"low sodium"* result of 123 mmol/L.**

I knew the sodium result was not accurate on the analyser after heparin was added to the sample. It did lead me to reassessing his fluids and decreasing the rate of 0.18NaCl/4%Glucose.

(b) **State whether you considered checking the serum sodium by laboratory analysis following the *"low sodium"* result of 123 mmol/L. If so, state the outcome of your consideration. If not, explain why.**

I considered at that stage I would perform a sodium level at the end of the operation.

(42) Answer to Question 28(a) at p.14:

"Myself and the anaesthetic trainee [were aware that Adam had sodium levels as low as 123mmol/L]."

(a) **Explain when and by what means *"the anaesthetic trainee"* was *"aware that Adam had sodium levels as low as this [123mmol/L]".***

I would have discussed during the case my examination of the medical records with the trainee.

(43) Answer to Question 28(d) at p. 14:

"The outpatient clinic letter from Dr. Savage (057-056-114, 115) records no ill effects."

(a) **Identify where in the *"outpatient clinic letter from Dr. Savage (057-056-114, 115)"* is it recorded that there were *"no ill effects."***

The absence of any recorded ill effects in the letter is what I meant to convey. I could have written, the letter did not record any ill effects.

(44) Answer to Question 29(b) at p.14:

"Reassessment is a continuous process and relates to continuing monitoring as recorded in the anaesthetic record (058-003-005). Myself and the anaesthetic trainee were involved and the conclusion was that the appropriate amount of fluid was being delivered."

(a) **Explain exactly in what way the *"anaesthetic trainee"* was *"involved"* in the *"review [of] the fluid management, blood loss"*, and in particular describe what he or she actually did.**

The anaesthetic trainee and/or myself were present throughout the operation and I prescribed and administered the fluid. The trainee was under my supervision.

(45) **Answer to Question 29(c) at p.15:**

"When the new kidney was connected we looked to see if it was getting sufficient blood, ie was the blood pressure sufficient to perfuse it, which it appeared to be."

(a) Identify the persons to whom you refer when you state *"we looked..."*

Myself and the trainee anaesthetist.

(b) In relation to *"we looked to see if it was getting sufficient blood"*, state if you visualised the transplanted *"new kidney"* directly in order to make this assessment. If not explain what you mean by *"we looked to see"*.

Yes I visualised the transplanted kidney and could see its colour and perfusion state.

(c) Explain what happened to the CVP pressure reading when the clamps were released, giving figures before and after this event.

Before release 22 mmHg, after release 20 mmHg

(d) State if you consider that there would have been any reason, other than insufficient blood pressure, for the donor kidney not to perfuse well after release of the vascular clamps. If so explain any other factors that would have produced that effect..

Other reasons could have been lack of oxygen in the blood (his oxygen levels were normal), spasm or thrombosis of the artery, or a poorly functioning kidney graft.

(46) **Answer to Question 29(e) at p.15:**

"Myself and the anaesthetic trainee [administered the Prednisone and Azathioprine]"

(a) State exactly what *"the anaesthetic trainee"* did in relation to administering the *"Prednisone and Azathioprine"*.

I did not record who administered the drugs. It would have been myself or the anaesthetic trainee.

(47) **Answer to Question 29(f) at p. 15:**

"We were satisfied that the vital signs were adequate and appropriate."

(a) Specify the *"vital signs"* to which you refer, and their measurement which you considered *"were adequate and appropriate."*

The oxygen saturation level, end tidal carbon dioxide, Heart Rate, Blood pressure and CVP levels.

(48) **Answer to Question 30(c) at p. 15:**

"The fluid reassessment is explained in the remainder of this paragraph. [WS-008/1 page 6 2(iii)]"

(a) You have not adequately answered the question. Please explain what you concluded from that reassessment, what action was taken in the light of it and by whom.

As stated at WS-008/1 page 6 2(iii) point 1 (NaCl/Glucose had been given to replace the amount lost by Adam's native kidneys and provide maintenance sugar requirements), point 2 (HPPF and Blood had been given to replace that lost and help to restore low haemoglobin) and point 3 (Hartmann's solution was commenced to maintain the CVP and provide the new kidney with sufficient preload to ensure its

function). These were the conclusions from the reassessment and the action taken by me and the trainee.

(49) **Answer to Question 31(b) at p.15:**

"Myself and the anaesthetic trainee were investigating the reasons why he did not wake up. The vital signs were continued and recorded on the monitor to just before transfer to PICU at 11.45 (058-008-023, 024)"

(a) Describe what *"the anaesthetic trainee"* actually did by way of *"investigating the reasons why [Adam] did not wake up"*.

The trainee performed a muscle stimulation test to see if the muscle relaxants had worn off as a possible cause of Adams failure to wake up. The muscle test was normal.

(50) **Answer to Question 33(a) at p.16:**

"I rechecked the blood loss measurements. (058-007-021)"

(a) You have not adequately answered the question. Please state the estimate made of the losses on the towels and on the floor and explain how that estimate was made.

This was a visible estimate and no accurate measurement was taken. My estimate was greater than 300 mls. (058-003-005)

(b) Explain how much the swab weighing was affected by urine (from the opened bladder), peritoneal fluid (from the previous peritoneal dialysis), and ice slush.

The bladder was not opened until near the end of the operation. The swabs would have contained only blood until that time. I was not aware of any significant fluid from the previous peritoneal dialysis or ice slush. The bladder contents would have been suctioned during the opening of the bladder.

(c) In the light of the above comments, state and explain how accurate you think your blood loss estimate was.

I think my estimate of blood loss was as accurate as in answer 50 (a).

(51) **Answer to Question 33(b) at p.16:**

"It confirmed approx 911mls of blood [was lost during surgery]"

(a) State: (i) who recorded, in the Fluid Balance and Intravenous Fluid Prescription Sheet (Ref: 057-018-026), the theatre fluid intake of 3000 mls and the theatre blood loss of over 1200 mls; and (ii) from where those figures were obtained.

It would have been a PICU nurse. I do not know where these figures were obtained.

(b) State from where you produced a blood loss figure of 1128 mls in your Deposition (Ref: 011-014-097).

This was calculated from the swabs, suction and towels. (058-003-005)

(52) **Answer to Question 33(c) at p.16:**

"I believed that I had corrected his deficit, provided maintenance and met his losses as well as preparing his circulation for a kidney transplant, as planned."

(a) **Specify and explain your fluid management plan developed for Adam before the case started, including the content, volume and rate of fluids to be administered.**

I had planned to replace Adams deficit of 400 mls and administer fluids at a maintenance rate 200 mls/hr and also to administer fluids HPPF and Hartmanns to increase his circulating blood volume prior to the new kidney. I had planned to adjust the rate of fluids in response to on-going losses and observation of his HR, BP and CVP.

(b) **State what was actually administered (including content, volume and rate of fluids) and whether or not that corresponded to your plan. If it did not correspond to your plan, explain the reasons why not.**

I administered 500 mls of 0.18%NaCl/4% Glucose initially and then erected another 500 mls to run after this in the first hour. (058-003-005)
I administered HPPF 400mls+400mls and 500 mls of Hartmanns solution to increase his circulating blood volume. (058-003-005)
I administered 2 units of Packed Blood cells to correct his anaemia during the operation. This corresponded to my fluid plan as I had expected to have to adjust the rate of fluids in response to on-going losses and observation of his HR, BP and CVP.

(53) Answer to Question 34(c) at p.17:

"Myself and the anaesthetic trainee [were administering fluids to Adam with the express purpose of increasing his blood volume]"

(a) **Describe what *"the anaesthetic trainee"* actually did by way of *"administering fluids to Adam with the express purpose of increasing his blood volume"***

The anaesthetic trainee would have administered the fluids that I had prescribed.

(b) **State what particular fluids you administered *'with the express purpose of increasing his blood volume'*. State when you administered them, and why they were administered at that time.**

HPPF was given to increase his blood volume at approx. 8.30hrs, Hartmanns was given to continue to increase his blood volume at approx 8.45-9.00hrs, and a further HPPF was given to increase his blood volume at approx 9.15hrs. (058-003-005).

(54) Answer to Question 37(a) at p.18:

"I cannot remember who [I worked with to determine the cause of Adam's death]. It would have been with the nephrologists and anaesthetists in PICU."

(a) **State whether you were present during Adam's autopsy and if so: (i) for how long you were present; (ii) the circumstances in which you came to be there; (iii) exactly what was discussed between yourself and Dr. Alison Armour, the pathologist.**

I do not remember being present at his autopsy.

(b) **State whether it was you who filled in Adam's autopsy request form (copy attached, Ref: INQ-0343-11). If not, state who filled in this document.**

The page provided labelled INQ-0343-11 is not an autopsy request form. It was not completed by me and I do not know who completed it however the initials AA suggest it was completed by Dr. Alison Armour (State Pathology).

(c) **If you did fill in the autopsy request form, explain what you meant by *"osmotic***

disequilibrium syndrome". **State if you still consider this to have been a possible cause of Adam's death. If so, explain your reasons why. If not, explain why.**

The words "osmotic dysequilibrium syndrome" do not appear on INQ-0343-11.

(d) Explain what you meant by Adam being *"a somewhat bizarre case of a child undergoing renal transplantation"* and explain the basis on which you formed that view.

I have been unable to identify the context when I made this statement.

(e) State whether you were in the operating theatre whilst the inspection and examination of the equipment by Dr. Fiona Gibson was taking place. If so: (i) explain for what purpose; (ii) state for how long (iii) state what if anything was said between you and Dr. Fiona Gibson and (iv) identify any other person/s present during that inspection and examination and the reasons for their presence.

I was not present during this visit.

(f) State whether you signed the log for the anaesthetic equipment (Ref: 011-004-014) immediately prior to Adam's surgery and if not, why not.

It was not practice for the anaesthetist to sign the anaesthetic machine log, see WS-008/2 Page 30 Q76d.

(55) **Answer to Question 37(d) at p.18:**

"To improve my documentation of fluid calculations and administration to children undergoing anaesthesia. Following Adam's death there has been improved reliability for testing of electrolytes in the operating theatre which assists the monitoring of fluid and electrolyte administration."

(a) Describe in what way, as a result of the knowledge learned from Adam's death, you have *"improve[d] your] documentation of fluid calculations and administration to children undergoing anaesthesia."*

I ensure to retain all fluid calculations in the anaesthetic record sheet since Adams case.

(b) Describe and explain in what way, as a result of the knowledge learned from Adam's death, *"there has been improved reliability for testing of electrolytes in the operating theatre which assists the monitoring of fluid and electrolyte administration"*, including an explanation of how the current position differs from that at the time of Adam's transplant surgery

The blood gas analyser now has more reliable sodium and potassium results and dry heparin crystals are now used to remove the diluting effect of heparin. A pneumatic tube system is now used to take samples to the biochemistry lab.

(56) **Answer to Question 38(b) at p.18:**

"It was with my anaesthesia colleagues in the weeks following Adam's death [that I worked to investigate Adam's death]."

(a) Identify the anaesthesia colleagues to whom you refer.

Dr Gaston, Crean and McKaigue.

(b) Describe what you investigated in relation to each of the following:

I have no records of the investigations to each of the following.

(i) **Fluid management**
(ii) **Epidural**
(iii) **invasive monitoring, including CVP**
(iv) **anaesthetic & monitoring equipment**
(v) **patient safety during anaesthesia**
(vi) **blood gas machine monitoring of serum electrolytes**

(57) **Answer to Question 38(c) at p.18:**

"[Adam's death] was never fully explained in my view."

(a) Please: (i) state what you believe the possible explanation for Adam's death to be; (ii) state which reason/s you believe to be the most likely; and (iii) provide the reasons for your belief.

I still do not have a clear explanation for Adams death. The cases of dilutional hyponatraemia described by Arieff were all related to children with intact ADH secretion and response. Unlike these children Adam was unable to concentrate his urine under the control of ADH. A recent case report from the Pediatric Nephrology journal describes a child with polyuria who died following a kidney transplant. There are similarities between this case and Adam's and it offers an explanation of Adam's death. *(Cansick J, et al. A fatal case of cerebral oedema with hyponatraemia and massive polyuria after renal transplantation. Pediatr Nephrol (2009) 24:1231-4)*

(58) **Answer to Question 39(b) at p.19:**

"The draft recommendations of 19.06.1996 (060-018-036) had the agreement of all the paediatric anaesthetists so became substantive from 20.06.1996 (060-014-025). They had been agreed by all the paediatric anaesthetists who were involved in major paediatric surgery so did not require further dissemination."

(a) Identify *"the paediatric anaesthetists"* who agreed the *"draft recommendations of 19.06.1996"*.

Myself and Drs Crean and McKaigue

(b) State who was responsible for co-ordinating the input of *"the paediatric anaesthetists"*

Dr Gaston

(c) Explain what you mean by *"major"*.

This refers to operations where invasive monitoring is required and there is blood loss anticipated to require transfusion.

(d) Explain the basis for restricting the draft recommendations to *"paediatric surgery"* only.

We did not have the experience to write recommendation for adult surgery.

(e) Explain the basis for restricting the draft recommendations to *"paediatric surgery"* which was major.

This was reflective of Adams case.

(f) Please clarify the process by which the draft recommendations *"became substantive"*, and what was the effect of them becoming *"substantive"*

No revision of the draft occurred and the paediatric anaesthetists all agreed with the content.

(g) State what was done with the draft recommendations once they became *"substantive from*

20.06.1996"

The paediatric anaesthetists agreed to act according to the recommendations.

(59) **Answer to Question 40(a) at p.19:**

"I do not have records of my teaching but would teach about fluid maintenance rates, fluid types and replacement fluids as contained in textbooks ..."

(a) If you have ceased to teach, please state when that happened

I continue to teach.

(b) From the texts cited identify the support for:

(i) the calculations that you made for Adam's pre-operative fluid management, including the type of fluid and rate of administration

(ii) the fluid that you administered to Adam during his transplant surgery and the basis for the type and rate,

The textbooks that I have cited did not offer any advice on the management of a child with polyuric renal failure undergoing kidney transplant.

(60) **Answer to Question 48(a) at p.22:**

"The U&E results of the sample taken at 9.30pm on the 26th November 1995 and recorded at 11.00pm were within normal limits."

(a) State: (i) what you would consider to be *"normal limits"* for serum sodium in a 4 year old child and; (ii) what you would consider to be *"acceptable limits"*.

The normal limits are 135-145 mmol/l. Acceptable limits may differ from this if the basis of the sodium level is chronically deranged. Every case needs to be considered in respect of the patients history and diagnosis.

(61) **Answer to Question 48(b) at p.22:**

"Dr. Savage prescribed bicarbonate and calcium supplements (093-006-015)"

(a) Explain why you think that Adam's pre-operative medication included *"bicarbonate and calcium supplements"*.

These supplements were prescribed by the Paediatric Nephrologists. They were given to improve bone development.

(b) State if you think that these were given to Adam preoperatively. If so, state why. If not, explain why not.

Adam was fasting from 05.00 so these would not have been given on the day of surgery.

(62) **Answer to Question 52(b) at p.23:**

"If the CVP line insertion and the epidural had taken less time a U&E sample could have been sent earlier"

(a) State the time at which each of the following were completed:

(i) **insertion of the epidural**
(ii) **insertion of the CVP catheter**

There is no record of the times when these procedures were completed. The CVP trace commences when the CVP line was inserted before 08.00.

(b) Explain how the time it took to complete the insertion of the CVP and epidural resulted in Adam's U&E not being sent until 09.32

It was because Dr Montague and myself were both occupied in our close observation of Adams anaesthetic.

(c) Explain when you would ordinarily have expected to complete the insertion of the CVP and epidural, assuming you induced anaesthesia at 0700.

It can take a variable amount of time and is dependent on individual patients. Ordinarily it would take about 1 hour to insert the iv, arterial line, CVP and epidural.

(d) Identify who would have taken the U&E sample for testing

Myself or the anaesthetic trainee.

(63) Answer to Question 54(a) at p.25:

"[The new kidney] looked dusky indicating that it was not getting sufficient perfusion"

(a) You have not adequately answered the question. Please explain what you meant by the *"new kidney did not work"*

It did not become pink when the clamps were released.

(64) Answer to Question 54(b) at p.25:

"Myself and the anaesthetic trainee [thought that we had underestimated fluid and we gave a fluid bolus at 9.32]"

(a) State the basis upon which you say that the *"anaesthetic trainee"* thought *"we have underestimated fluid"*

This was based on the review of his fluids and his HR, BP and CVP readings.

(b) Describe what *"the anaesthetic trainee"* actually did by way of the administration of the *"fluid bolus at 9.32".*

HPPF had been started just before this (09.15) to increase his circulating blood volume and this was continued as a fluid bolus.

(c) Explain why you 'thought we had underestimated fluid' at about 0930.

This was based on the review of his fluids and his HR, BP and CVP readings.

(65) Answer to Question 55(b) at p.24:

"a different analyser"

(a) Identify the particular *"different analyser"* that is now used in response to the *"common practice in the RBHSC"* and state when the *"different analyser"* was introduced

The AVL analyser is now used. It was introduced after Adams death. I do not know the date it was introduced.

(b) **Explain:**

(i) **the differences between the *"different analyser"* and that in use at the time of Adam's transplant surgery**
(ii) **how those differences address your claim that you *"would not rely on the machine to accurately analyse sodium levels"* [Ref: 011-014-108]**

The analyser in use at the time of Adams death did not provide accurate sodium levels as it used whole blood samples and heparin was added to prevent clots. The different analyser used now does produce reliable sodium levels with the use of syringes containing heparin crystals.

(66) **Answer to Question 55(c) at p. 24:**

"When I became a consultant in February 1991 I became aware of the practice."

(a) **State how you *"became aware of the practice"* when you *"became a consultant in February 1991"*.**

See answer WS-008/2 page 40 Q104

(67) **Answer to Question 56(f) at p.25:**

"[Adam's bladder being opened] led to a review of the fluids."

(a) **You have not adequately answered the question. Please describe and explain the *"effect on your calculations of Adam's 'bladder being opened'"***

Adams bladder was opened towards the end of the operation. This was another opportunity to assess Adams losses and fluid administration.

(b) **Describe what you did by way of a *"review of the fluids"***

I checked the blood losses in the swabs, suction and towels and compared this to his HR, BP and CVP and to the fluid and blood that I had administered.

(c) **State the outcome of the *"review of the fluids"* after Adam's bladder was opened, and where this *"review"* is recorded.**

There is no record of this review, it is my standard practice.

(68) **Answer to Question 57(a) at p.25:**

"I was aware of the effect of SIADH in anaesthetised patients prior to Arieff's paper. It was my practice to use balanced salt solutions in anaesthetised patients with intact ADH/renal function with the exception of small infants who needed glucose infusion."

(a) **Explain what you mean by *"balanced salt solutions"*.**

0.9%NaCl and Hartmanns solution are balanced salt solutions. Balanced salt solutions are produced so that they are very close to being isotonic and iso-osmolar.

(b) **State what crystalloid fluid you would have used for (i) maintenance; and (ii) blood loss replacement in November 1995 in:**
- **healthy infants**
- **healthy children undergoing surgery**

In 1995 I would have used 0.18NaCl/4% Glucose solution at maintenance rates for healthy infants and

healthy children undergoing surgery.
For blood loss in both healthy infants and children undergoing surgery I would have used Hartmanns solution initially. If the blood loss exceeded 20% of the circulating blood volume I would check the haematocrit and give a blood transfusion.

(69) **Answer to Question 58(a) at p.25:**

(a) You have not adequately answered that question. Please explain how Arieff's BMJ 1992 paper *"was relied upon to reach the statement [at C5 - Ref: 011-014-107a] in respect of 'patients undergoing major paediatric surgery who have a potential for electrolyte imbalance'"*

Arieff described a series of cases where increased ADH secretion led to a concentrated, low volume urine (oliguria). In such cases the water retention by the kidneys causes the sodium to fall rapidly in the blood leading to dilutional hyponatraemia.

(70) **Answer to Question 59(a) at p.26:**

"[There has to be 3 nurses present before an anaesthetic is commenced] This was the procedure. One nurse for the anaesthetist, one as the scrub nurse and a runner."

(a) Explain the *"procedure"* to which you refer.

The procedure is the term I gave to the usual practice among nursing staff. The requirement was for a minimum number of staff to be present before an operation would commence.

(b) Explain the basis of your statement that *"there has to be 3 nurses present before an anaesthetic is commenced"*. Identify any guidelines/protocols/teaching which existed in 1995 that stated this and if there are none, please identify the source of your statement.

This was their usual practice.

(c) State if there were three nurses present before the anaesthetic was commenced in Adam's case and explain the basis for your belief. If not, explain why you induced anaesthesia.

I believe there were two qualified nurses and a nursing auxillary and they indicated that I could begin the anaesthetic.

(d) State if there was an anaesthetic nurse assisting you in addition to the Medical Technical Officer, Mr Peter Shaw. If not, state whether there should have been.

Yes, one of the qualified nurses was my anaesthetic nurse.

(e) Describe what the duties of an anaesthetic nurse would/should have been in relation to Adam's care.

The anaesthetic nurses duties were to prepare the anaesthetic equipment provide drugs for me to draw up including controlled drugs and to confirm the patient's identity and preoperative checks. Following this the nurse would assist me in the venepuncture, intubation and anaesthetic procedures, arterial line, CVP and epidural.

(f) State whether it was normal practice for an anaesthetist to have the assistance of an Medical Technical Officer in addition to an anaesthetic nurse in 1995 at the RBHSC.

Yes it was normal practice to have an MTO in addition.

(71) **Answer to Question 62(a) at p.27:**

"[I linked up with] Consultant paediatricians and anaesthetists with an interest in paediatrics [at Altnagelvin and Causeway]."

(a) **Identify the *"consultant paediatricians and anaesthetists with an interest in paediatrics"* you *"linked up with"* at *"Altnagelvin and Causeway"*.**

Drs Brown (paediatrician) and Stewart (anaesthetist) in Altnagelvin and Dr Ledwith (paediatrician) in Causeway hospital

(72) **Answer to Question 63(b) at p.27:**

"Dr O'Connor was available on the morning of Adams transplant and was in theatre. I cannot remember how long she was with me."

(a) **You have not adequately answered the question. Please state what your *"close consultation"* with Dr O'Connor entailed and where it took place.**

Dr O'Connor did come into theatre. I have no record of the conversation with her. She gave me instructions to administer the prednisolone and azothiaprine when the clamps were released on the new kidney.

(b) **If your *"close consultation"* took place in theatre, state whether Dr. O'Connor was gowned or not.**

I cannot recall if she was gowned or not.

(73) **Answer to Question 64(a) at p.27:**

"The surgeon can request that more fluid is given if he wants more perfusion or urine output."

(a) **Explain who you consider has the final say as to whether fluid is administered in a situation where the surgeon requests more fluid is given (e.g. to increase kidney perfusion) and the anaesthetist present believes this to be inappropriate.**

It is generally a joint decision with both anaesthetist and surgeon discussing the fluids to give at this time.

(b) **State whether Mr. Keane or Mr. Brown asked for more fluids, and if so, state at what time or at what stage in the surgery and for what reason.**

I cannot remember if they requested more fluids at this time.

(74) **Answer to Question 65(a) at p.28:**

"His diagnosis was 'bilateral dysplastic kidneys with large cysts' ... and 'reflux nephropathy' ... not as I suggested"

(a) **You have not adequately answered the question. Explain fully the basis of your assertion that Adam's condition was one of *"congenital nephrotic syndrome"***

Adam did not have congenital nephrotic syndrome.

(75) **Answer to Question 72(a) at p.29:**

"From his medical records on 9/11/1995. "Feeds Gastrostomy (button) 3x200 bolus 1500ml O/N ?how many calories - 1540 kcals = 77kcal/kg Sucks bread. No feed." (058-035-143)"

(a) **You have not adequately answered the question. Please state whether you mean that Adam suffered from *"poor nutrition"* and *"poor weight gain"* as a result of his renal problems.**

It was apparent to me that Adam needed assistance with the provision of his nutrition when I read this entry in his medical records. This required him to have a gastrostomy and night feeds.

(76) **Answer to Question 72(b) at p.29:**

"Adam did not take sufficient nutrition during the day. His overnight nutrition given by gastrostomy button ensured weight gain. The effect was that I had to continue to provide glucose to prevent hypoglycaemia."

(a) **Explain why you believed that Adam could not manage without a calorific intake over the 4 hours of the operation.**

This was routine practice at that time as there were reports of hypoglycaemia prior to 1995.

(b) **State whether normal saline with 4% dextrose was available in RBHSC on 27th November 1995.**

It was not available.

(c) **List the clinical studies which show that children (excluding infants) require glucose during surgery to maintain normal blood glucose concentrations.**

O'Flynn PE and Milford CA. Fasting in children for day case surgery. Annals of the Royal College of Surgeons of England (1989); 71: 218-9

Thomas DKM. Hypoglycaemia in children before operation: Its incidence and prevention. Br J Anaesth 1974;46:66-8

Maze A, Samuels SI. Hypoglycaemia-induced seizures in an infant during anaesthesia. Anesthesiology 1980;52:77-8

Jensen BH, Wernberg M, Ansersen M. Pre-operative starvation and blood glucose concentrations in children undergoing in-patient and out-patient anaesthesia. Br J Anaesth 1982;54:1071-4

(d) **Identify those (providing the relevant citation) which support your view that you *"had to continue to provide glucose to prevent hypoglycaemia."***

This was routine practice and is supported by evidence in answer 76(c).

(77) **Answer to Question 74(a) at p.30:**

"[The research] involved checking [Adam's] notes, [and] looking for or researching relevant information about his previous anaesthetics"

(a) **You have not adequately answered the question. Please describe and explain the information you obtained through those researches and its significance to your plans for your management of Adam prior to and during his transplant surgery.**

I looked at his previous anaesthetic records for any difficulties other anaesthetists had recorded such as management of his airway or venous access.

(78) **Answer to Question 76(d) at p.30:**

"Routine checks [of equipment] were not recorded"

(a) **Explain the requirement for recording pre-operative equipment checks, including**

providing any rules, protocols or guidance
The Association of Anaesthetists of GB & Ireland, Monitoring Standards

(79) **Answer to Question 77(d) at p.31:**

"[The decision to replace Adam's fluid deficit within a 30 minute period] was to replace the type and volume of fluid that he would have usually required. There was an urgency to replace this deficit and provide sufficient maintenance fluid."

(a) **Explain why you considered there was an *"urgency"* to provide 500 ml of fluid within the first half-hour after induction of anaesthesia.**

I needed to correct his fluid deficit as quickly as I was able before I began the process of increasing his circulating blood volume prior to his kidney graft and taking into account the long cold ischaemic time.

(80) **Answer to Question 77(e) at p.31:**

"[My statement that we hadn't fully replaced Adam's deficit and his first hour's maintenance] was based on my concerns for his deficit (around 300mls) and requirement for a further 150mls in that first hour and to ensure that no potential deficit remained as we began the process of increasing Adam's circulating blood volume (hypervolaemia) in preparation for his kidney transplant."

(a) **Explain in detail your reasons for giving Adam approximately 800ml of 1/5 normal saline between 0700 and 0815 prior to surgery starting.**

To replace his fluid deficit and replace the large volume of dilute urine he was passing.

(b) **In particular, state whether you were attempting to expand Adam's vascular volume and, if so, explain in detail your reasons for doing so at this time.**

No

(c) **Explain the meaning of *"we began the process of increasing Adam's circulating blood volume (hypervolaemia) in preparation for his kidney transplant"*, and the reasons why you began that process.**

HPPF and Hartmanns were used to expand his blood volume starting after the first hour.

(d) **Specifically, state the time at which you *"began the process of increasing Adam's circulating blood volume (hypervolaemia) in preparation for his kidney transplant"***

After I had completed the anaesthetic procedures and the surgery had commenced around 8am.

(e) **State whether you considered Adam's intravascular volume to be inadequate and if so, state the objective signs thereof and the reasons for your view. If not, explain why not..**

I considered his blood volume to be adequate because he had a normal BP. I was however aiming to increase his blood volume prior to his kidney transplant in the presence of a large volume of dilute urine.

(81) **Answer to Question 79(a) at p.32:**

"I had to consider transfusing [Adam] with blood because of increasing blood loss."

(a) **You have not adequately answered the question. Please explain what precipitated the *"blood loss"* becoming *"quite problematic"*.**

He had lost around 400 mls of blood which was 25% of his estimated blood volume (1600 mls). I did a haematocrit level that confirmed that he required a blood transfusion. This was problematic as it meant that checking of blood and preparing it for transfusion was required which further occupied my time with the anaesthetic trainee.

(82) **Answer to Question 81(a) at p.32:**

"I meant [by Adam was exceptional] that Adams native kidneys were losing exceptional or unusually large volumes of urine."

(a) Explain how coping with 300 mls of Solution No.18 in an hour equates to being able to cope with 500 mls of the same solution in half an hour.

The operation where he received 300 mls of 0.18NaCl/4%glucose was not for a kidney transplant so there was not the requirement to correct the deficit and make him hypervolaemic.

(83) **Answer to Question 83(a) at p.33:**

"A volume of 20mls/kg of crystalloid, balanced salt solution is commonly given for hypovolaemia or circulatory shock."

(a) State if you believed Adam to be in a state of *"hypovolaemia or circulatory shock"*, and if so, indicate the evidence for this belief in: (i) the clinical notes; (ii) elsewhere.

I did not believe Adam was hypovolaemic. I was referring to the practice in paediatric life support for children who are hypovolaemic.

(84) **Answer to Question 84(a) at p.33:**

"[The evidence suggested that Adam was already dehydrated] because he had ongoing losses of dilute urine as well as maintenance requirements."

(a) State what evidence you had of Adam's dehydration, other than what you say are Adam's usual fluid requirements.

I believe I had meant to say that Adam had a deficit rather than he was dehydrated.

(b) State whether Adam showed any symptoms or signs of dehydration and if so: (i) describe what they were; and (ii) where they are recorded.

Adam did not show any signs of dehydration. These signs may not show up until the child has lost 5-10% of their body weight. In Adams case this would correspond to 1000-2000mls. I did not expect Adam to become this dehydrated. My plan was to ensure that there was no element of dehydration.

(85) **Answer to Question 86(b) at p.33:**

"[Adam's] vital signs, HR, BP and CVP had not responded to the fluids given up to that time. As fluid is infused I would have expected an increase in BP and/or a fall in HR."

(a) If Adam was hypovolaemic, state the effect on heart rate (HR) and blood pressure (BP) that you would expect following the administration of fluids.

I did not believe that Adam was hypovolaemic. It was my aim to make him hypervolaemic. Normally the heart rate would increase and the blood pressure decrease if Adam was hypovolaemic. Adam received atropine at induction of anaesthesia and this increased his HR.

(b) **If Adam was normovolaemic, state the effect on heart rate (HR) and blood pressure (BP) that you would expect following the administration of fluids.**

If a patient is normovolaemic and I am aiming to make them hypervolaemic I would expect the heart rate to decrease and the blood pressure to increase.

(86) **Answer to Question 87(b) at p.34:**

"[The observation that the wound does or does not look 'moist'] allows an assessment of immediate changes to the circulating blood volume before it is detected by weighing swabs."

(a) **Explain in detail how looking at a wound *"allows an assessment of immediate changes to the circulating blood volume"*.**

In a kidney transplant the iliac vessels can be seen. If the iliac vein or artery or their branches are very narrow then it can give an indication of the state of the circulation.

(87) **Answer to Question 88(b) at p.34:**

"Previous surgical ligation of the jugular vein from a previous Broviac Central venous line would have caused an obstruction in this vein."

(a) **State from where you derived the information that there had been a *"previous surgical ligation of the jugular vein"* and when.**

From his operation note (050-008-032) undated.

(b) **State whether you took account of any compensatory enlargement of all alternate pathways which may have developed between May 1992 and November 1995 following the *"previous surgical ligation of the jugular vein"* and if so, how. If you did not do so, explain why not.**

I did take account of other possible central veins but was successful at cannulating his right subclavian vein.

(c) **Given Adam's history, state whether as part of the preparation for Adam's transplant, any ultrasound examination was made of the veins in his neck to identify those which remained patent, and if so, state when this was done and the outcome and records of that examination. If this was not done, state the reasons why not.**

Ultrasound was not done on the morning of surgery. If I had not been successful in cannulating his right subclavian vein I would have requested one.

(88) **Answer to Question 88(c) at p.34:**

"Myself and Dr Montague knew there was a previous Broviac line scar."

(a) **State the basis on which you concluded that the scar on Adam's neck was from a previous Broviac Central venous line.**

From his operation note (050-008-032)

(b) **State the basis for your assertion that Dr. Montague: *"knew there was a previous Broviac line scar."***

Dr. Montague and I worked together.

(89) **Answer to Question 90(b) at p.35:**

"[The basis for my approach of pushing the CVP to "15, 16, 17" was to expand the circulating blood volume (hypervolaemia) in advance of the kidney transplant."

(a) Explain the reasons why *"pushing the CVP to "15, 16, 17""* would have been appropriate in Adam's case

Because the tip of his CVP line was not in the Superior Vena Cava so it was not giving an accurate reading.

(b) State the clinical literature / guidelines / protocols supporting your *"approach of pushing the CVP to "15, 16, 17".*

I cannot find literature relating to this matter prior to 1995. However there is a reference to this in a publication since then.

In the case report from Pediatric Nephrology the CVP was 10-15 during the kidney transplant.
(Cansick et al. A fatal case of cerebral oedema with hyponatraemia and massive polyuria after renal transplant. Pediatr Nephrol (2009) 24:1232.)

(c) State in what circumstances, other than fluid overload, would a CVP reading of 17 mmHg have been appropriate:

(i) in paediatric surgery
(ii) at all

The CVP can be raised for the following reasons in "paediatric surgery and at all";
SVC obstruction, cardiac tamponade, heart failure, pleural effusion and certain congenital heart diseases. *(Hatch and Sumner, Paediatric Anaesthesia 1999. P380 "superior vena cava pressures.....in the range of 10-15 mmHg")*

(d) Identify the documents that record *"when [Adam] was taken to the PICU ... his CVP was 10-12 mmHg"* as stated in your Deposition (Ref: 011-014-101)

058-008-022

(90) **Answer to Question 95(a) at p.36:**

"Obtaining the blood test was not considered an urgent priority and it was done in sequence when time permitted. I did not consider I needed to divert one of the team or ask another doctor to do the test."

(a) State the reasons for your statement that *'the blood test was not considered an urgent priority'.*

Close monitoring and inserting the arterial line, CVP and epidural were the main clinical priorities that made the blood test a less urgent priority.

(b) Describe the *"sequence"*, state where in that sequence *"obtaining the blood test fell"* and explain your reasons for its ranking

The sequence meant that these procedures were done one at a time which involved a sterile area and positioning of the patient. I did not record the sequence of procedures. Usually the endotracheal tube placement would be followed by the venous line insertion, then the arterial line, then the epidural and then the CVP line. The priority for blood test was after these procedures.

(c) State when the first occasion was that *"time permitted"* the blood test to be taken, and

explain why time did not permit a blood test at any earlier stage

9.30 was when the first blood test was done. Before that time myself and Dr Montague were occupied by monitoring Adam and performing the procedures.

(d) State if you considered asking a nurse or technician from outside the operating team to attend the operating theatre to take a blood sample down to the lab for testing. If you considered this, state why you did not do so. If you did not consider it, state why not.

No, the sample was taken and analysed when I considered it necessary.

(e) Describe what, if any, knowledge you had in 1995 of the portering service available on 26th and 27th November 1995 to the theatre in RBHSC for tasks including the transporting of specimens to the laboratory.

I was aware that a porter would take a sample to the lab if requested. The service could be variable, including delay in contacting a porter, their arrival, and the time taken to take a sample to the lab.

(f) State whether or not you knew in 1995 if a pneumatic tube system was available in RBHSC on 27th November for samples from the theatre to be sent directly to the laboratory.

I knew no pneumatic tube system was available.

(g) State whether, in November 1995, the RBHSC had, or had access to, any portable blood gas analyser machines e.g. iSTAT blood gas analyser to measure sodium, potassium, urea, and creatinine. If so:

I do not know.

(i) identify the type of blood gas analyser was available at that time
(ii) state where it was located
(iii) state what arrangements would have been required for its use in Adam's transplant surgery
(iv) state the accuracy of the results for sodium compared to
(v) the static blood gas analyser
(vi) laboratory blood tests

(h) Other than the blood gas analyser machine model 1400 and the equipment in the laboratory for measuring serum sodium levels, state whether any other equipment was available to RBHSC in November 1995 to measure serum sodium levels, and if so:

(i) identify that equipment,
(ii) state whether or not it was portable
(iii) describe its location in RBHSC
(iv) state how long it would have taken that equipment to analyse a blood sample for sodium

I am not aware of any other equipment.

(i) Given that it had been agreed that a further blood sample be taken from Adam prior to surgery for U&E analysis, state what arrangements and provision you made pre-operatively to enable any blood sample to be transported promptly to the laboratory and/or a blood gas machine for analysis. If there were none made, explain why not.

None, I would only make transport arrangements just before the sample is taken.

(91) Answer to Question 96(b) at p.36:

"The technician is involved in the setting up of the CVP line, the radial arterial line and the epidural. The technician may have been the person who used the blood gas analyser in due course."

(a) State the primary purpose of carrying out the blood test on the blood gas analyser at 09:32, what specific information you required from that test and the reasons why you required that information at that time.

The Blood gas test was done to assess his pH, pO2, pCO2 and haematocrit. I required this information prior to his transplant to ensure that his new kidney would be optimally perfused.

(b) State the time at which you became concerned regarding Adam's serum sodium level and explain the reasons for that concern.

At the end of the operation when he did not wake up.

(92) Answer to Question 96(d) at p.37:

"Myself and Dr Montague were inserting an arterial line, epidural and CVP lines. Whilst one of us was concentrating on a task the other was ensuring continuous monitoring of [Adam's] vital signs and adjusting the anaesthetic. The technician was assisting with these procedures."

(a) State exactly what the technician was required to do by way of assisting you and Dr. Montague

He was required to prepare the anaesthetic machine and monitoring equipment including zeroing the arterial and CVP lines and attaching these to the monitors.

(b) Compare and contrast the duties of the Medical Technical Officer with those of an anaesthetic nurse.

The anaesthetic nurse is required to prepare anaesthetic equipment, endotracheal tubes, laryngoscopes, suction devices and sterile trolleys for procedures prior to the arrival of the patient in theatre, check the consent form and patient identity on arrival in theatre and assist the anaesthetist in the procedures, induction, intubation venous access, arterial access, epidural and CVP as well as taping and securing these devices and maintaining the child's temperature.

MTO is required to prepare the electronic monitors and anaesthetic machine prior to the childs arrival in theatre. The MTO also is responsible for the zeroing of the arterial and CVP lines and attaching these to the monitors

(93) Answer to Question 96(e) at p.37:

"The haematrocrit reading of 18 was the most significant result from this test result. It led to the preparation of a blood transfusion."

(a) State what serum concentrations you wanted analysed when you sent a blood sample to be analysed by the blood gas machine at 0930.

The blood gas analyser measures whole blood concentrations of pH, pO2, pCO2 and haematocrit. These were the parameters I wanted to check at 9.30.

(b) Please explain the significance for your fluid management if Adam's serum sodium concentration was 123 mmol/L at 0932.

If I had been able to rely on the accuracy of the sodium of 123 I would have stopped the 0.18 NaCl/4%Glucose and administered hypertonic saline.

(c) **State whether the decrease in haematocrit could have been caused by anything other than blood loss and, if so, explain what that cause might be.**

In that situation at 9.30 I had expected this haematocrit reading because he had lost 400 mls of blood corresponding to about 25% of his blood volume. Otherwise a low haematocrit could be due to the use of plasma expanders.

(94) **Answer to Question 97(b) at p.37:**

"[Identify the measurements of Adam's urine sodium concentrations to which you had access prior to his transplant surgery, giving in each case both the result and the date when it was received] Urine sodium 41 mmol/L recorded on 14.12.1991 (050-018-051), 34 mmol/L recorded on 28.11.1991 (050-018-055), 47 mmol/L recorded on 29.11.1991 (050-018-055), 52 mmol/L recorded on 30.11.1991 (050-018-055), 29 mmol/L recorded on 05.12.1991 (050-018-055)"

(a) **State whether you had any of the following urinary sodium results available to you at the time:**

- **19.12.91 (Ref: 049-030-178)**
- **20.12.91 (Ref: 049-030-182)**
- **02.01.92 (Ref: 050-024-163)**
- **06.01.92 (Ref: 050-024-185)**
- **09.01.92 (Ref: 050-024-176)**
- **08.02.92 (Ref: 050-024-222)**
- **12.02.92 (Ref: 050-024-214)**
- **14.02.92 (Ref: 050-024-211)**
- **17.02.92 (Ref: 050-024-209)**
- **26.02.92 (Ref: 050-024-225)**
- **25.03.92 (Ref: 052-025-074)**
- **29.05.92 (Ref: 053-028-084)**
- **02.12.92 (Ref: 054-059-167)**
- **17.11.93 (Ref: 055-054-134)**
- **16.12.93 (Ref: 055-054-161)**

These were in his medical notes and were available to me at the time.

(b) **If you did not have these available, state why, and if these results would have affected your calculations in any way. If you did have them available, explain why you did not state this previously.**

These were available. I cannot explain their previous omission.

(c) **State whether you consider that Adam's renal function and urinary sodium excretion were the same in November 1995 as in December 1993. If so, explain the reasons why. If not, explain the reasons why not.**

Over that period of time (2 years) there had been a change in Adams renal function so that he required dialysis. None of the above results were performed after 1993.

(95) **Answer to Question 98(a) at p.38:**

"I examined [Adam's] medical records in relation to previous anaesthetics, trying to identify any potential problems."

(a) **Identify which notes you examined in relation to Adam's previous anaesthetics.**

I would have examined his anaesthetic notes. The most recent anaesthetics would have provided the most relevant information regarding his current condition.

(96) **Answer to Question 100(a) at p.39:**

"Dilutional hyponatraemia as described by Arieff is the term given to administration of hypotonic fluids to a patient with increased ADH secretion which causes low volumes (oliguria) of concentrated urine leading to water retention and this excess free water causes the syndrome."

(a) You have not adequately answered the question. Please state what <u>you</u> understand by the term *"dilutional hyponatraemia"*

I understand this term as described by Arieff. It is due to the secretion and action of increased ADH on the kidneys which leads to water retention and low volumes of concentrated urine. The water retention combined with the administration of hypotonic iv fluids causes a fall in the serum sodium level.

(b) State whether you think that different forms of *"dilutional hyponatraemia"* exist depending on the cause.

I agree with Arieff's description of dilutional hyponatraemia. There are different causes of increased ADH secretion but its effect appears to be the mechanism of dilutional hyponatraemia as described by Arieff.

(97) **Answer to Question 100(b) at p.39:**

"Adam's kidneys were unable to concentrate urine even in the presence of increased ADH secretion so therefore could not retain free water and get dilutional hyponatraemia, the mechanism described by Arieff. This means I felt his death certificate was not accurate."

(a) State if you did anything about the fact that you considered that Adam's *"death certificate was not inaccurate"*. If so, state what you did. If not, explain the reasons why.

I was not able to do anything about the cause of death as decided by the Coroner on Adams death certificate.

(98) **Answer to Question 101(a) at p.39:**

"His theory [Arieff's] has been substantiated by several Randomised Controlled Trials, recently"

(a) Identify the *"Randomised Controlled Trials"* to which you refer and in each case state the date on which Arieff's 'theory' was *"substantiated"*.

In 2004 Mathur et al, "We found no randomised controlled evidence to show that use of isotonic saline as a maintenance fluid instead of a hypotonic saline will lead to an improvement in outcomes. Randomised trials with adequate design and sample sizes are needed to evaluate the possible advantages and risks of using isotonic saline as maintenance fluid." *(Mathur A ,et al. Hypotonic vs isotonic saline solutions for intravenous fluid management of acute infections. Cochrane Satabase Syst Rev. 2004;(2):CD004169.)*

Neville KA, et al. conducted an RCT looking at rehydration in children. They concluded, "In gastroenteritis treated with intravenous fluids, normal saline is preferable to hypotonic saline because it

protects against hyponatraemia without causing hypernatraemia." *(Neville KA, et al. Isotonic is better than hypotonic saline for intravenous rehydration of children with gastroenteritis: a prospective randomised study. Arch Dis Child. 2006 Mar;91(3):226-32. Epub 2005 Dec 13.)*

Choong K, et al. conducted a systematic review and concluded, "The current practice of prescribing i.v. maintenance fluids in children is based on limited clinical experimental evidence from poorly and differently designed studies, where bias could possibly raise doubt about the results. They do not provide evidence for optimal fluid and electrolyte homoeostasis in hospitalised children. This systematic review indicates potential harm with hypotonic solutions in children, which can be anticipated and avoided with isotonic solutions. No single fluid rate or composition is ideal for all children. However, isotonic or near-isotonic solutions may be more physiological, and therefore a safer choice in the acute phase of illness and perioperative period." *(Choong K, et al. Hypotonic versus isotonic saline in hospitalised children: a systematic review. Arch Dis Child. 2006 Oct;91(10):828-35. Epub 2006 Jun 5.)*

Yung M. and Keeley S. conducted an RCT of iv fluids and concluded, "Sick and post-operative children given dextrose saline at traditional maintenance rates are at risk of hyponatraemia." *(Yung M and Keeley S. Randomised controlled trial of intravenous maintenance fluids. J Paediatr Child Health. 2009 Jan-Feb;45(1-2):9-14. Epub 2007 Nov 25.)*

(99) **Answer to Question 103(a) at p.39:**

(a) You have not adequately answered that question. Please explain *"the mechanism by which Adam could have had 'an unlimited urine output'"*.

I knew that he was unable to concentrate urine because of his diseased kidneys and had a large volume of dilute urine. I was uncertain about what Adam's urine output was. I had thought that he could pass very large volumes in response to fluid.

(100) **Answer to Question 103(b) at p.39:**

"[My assertion that Adam could have had an unlimited urine output] was assumed from his intake of 200 ml/hr and the fact that his kidneys had the ability to pass large volumes of dilute urine."

(a) State how much urine you calculated Adam would have voided in the period from the induction of anaesthesia at 07.00 until the ureteric re-implantation was completed at approximately 10.30 and the basis of your calculations.

I estimated that he would have voided 200 ml/hour which would be 700 mls over this 3.5 hr period

(b) Describe the appearance and size of Adam's bladder when it was first exposed

I do not remember looking at the bladder when it was first exposed.

(101) **Answer to Question 104(a) at p.40:**

"Myself and the other paediatric anaesthetists [were continually warned by the medical technicians ... that we weren't to rely on these tests]."

(a) Identify the *"other paediatric anaesthetists"*.

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(b) Specify whether you were warned by the medical technicians not to rely on these tests in relation to sodium measurements at all or to any particular extent.

Yes because it was unreliable I did not rely on it at all.

(c) **State whether and how the blood gas analyser sodium measurement at 09.32 could have been used to inform Adam's fluid management during surgery, and explain the reasons for this. If it could not have been used, explain the reasons why not.**

The Analyser provided accurate haematocrit which informed me of the need to administer blood

(102) **Answer to Question 104(d) at p.40:**

"It was not highlighted as a particular problem because we would send a sample to the Royal Biochemistry Laboratory for accurate U&E tests"

(a) **State the normal turnaround time for laboratory analysis of serum sodium on 27th November 1995 between dispatching the blood sample to the laboratory and receipt of the result during:**

- **Normal working hours (weekdays 09.00 to 17.00)**
- **Out of hours (weekdays 17.00 to 09.00 or at weekends/holidays)**
- **In urgent cases, whether or not they arise within working hours**

I have no record of this. My recollection is that the time was variable depending on how long the porter took to arrive from his other duties and then take the sample to the lab. Normal working hours 30-90 minutes, Out of hours 30-120 minutes. These times refer to urgent cases as well.

(103) **Answer to Question 105(b) at p.40:**

"I remember mentioning [to Doctor Sumner and Doctor Savage] that Adam had high-output renal failure and so could not respond to ADH by concentrating urine and retaining water."

(a) **State what Dr Sumner and Dr Savage said in response to your comments.**

I have no record of their responses. I recall that they acknowledged that Adam would not respond to ADH to concentrate his urine.

(104) **Answer to Question 110(b) at p.41:**

"I cannot remember what was said [in respect of information that the kidney wasn't working well] but my response was to review the vital signs and the fluids."

(a) **State what action you took in relation to your review of *"the vital signs and the fluids"*.**

I checked his Heart rate, blood pressure and CVP levels.

(105) **Answer to Question 111(e) at p.42:**

"I assessed [Adam's] renal losses from his fluid allowance."

(a) **State what you mean by *"his fluid allowance"*.**

I meant his maintenance fluid rate and amount given during night feeds.

(b) **Explain in detail how you *"assessed [Adam's] renal losses from his fluid allowance"*.**

This was an assumption based on his fluid intake and his known large volume of dilute urine and fact that fluid was not removed during dialysis.

(106) **Answer to Question 112(b) at p. 42:**

"[Explain the basis for your assertion that the sodium of 123 at 9:32 was a "rogue result"]. The use of heparin made the sodium result unreliable."

(a) If you regarded the sodium result as *"unreliable"* and *"a rogue result"*, state why you responded to that result by *"drastically slow[ing] the rate of 0.18NaCl and commenc[ing] Hartmanns..."* (Ref: 059-004-007).

Even though I knew the sodium level on the analyser was inaccurate I re-examined my administration of 0.18NaCl/4%Glucose and reduced the rate of its administration from that time.

(107) **Answer to Question 118(a) at p.44:**

"[The failure of the kidney to 'pink up'] led to a reassessment of [Adam's] vital signs and fluid administration to ensure that I had corrected his deficit and produced a state of hypervolaemia."

(a) State what action you took following that *"reassessment"*.

I acted by reassuring myself that I had provided an increase in his circulating blood volume and that this was not a cause of poor kidney perfusion.

(108) **Answer to Question 118(c) at p.44:**

"[The long cold ischaemic time] meant that I had to proceed without delay to ensure that the transplant would have the best chance of success. This led me to administer the fluids quickly to replace [Adam's] deficit and begin the process of expanding his circulating blood volume, ie. Hypervolaemia."

(a) Explain why the *"long cold ischaemic time"* led you to *"administer the fluids quickly to replace [Adam's] deficit"*.

I thought that I should not cause any unnecessary delays in providing anaesthesia and related procedures and begin to prepare his circulation for the new kidney.

(b) State what effect a much shorter ischemic time would have had on the time over which you would have taken to replace the *"deficit"*.

If there had been less urgency in transplanting the kidney it is likely that I would have spent the necessary time in sending a blood sample.

(c) State whether you think that the fluids used for replacing the *"deficit"* and expanding the *"circulating blood volume"* could / should be the same? If not, explain why not.

Hartmanns, 0.9% NaCl and HPPF are given for expanding the circulation. 0.18NaCl/4%Glucose is not appropriate for expanding the circulation but will provide deficit replacement. Also in Adams case the sodium content of his urine was comparable to that of 0.18%NaCl so in his specific situation could replace his renal loss.

(d) State whether you discussed with the surgeons and/or Dr. Savage that there was a need to proceed expeditiously in view of the *"long cold ischaemic time"* of the donor kidney? If so, state: (i) when you discussed it; (ii) what their views were; (iii) what action was taken in relation to Adam's surgery; (iv) when that action was taken and by whom.

I have no record of these conversations. I recall that there was an urgency to get on with Adam's operation.

(109) Answer to Question 121(a) at p.45:

"I knew that [Adam] normally received around 150ml/hr input overnight which I would have expected to be matched with similar losses. His urine output is stated as "PU++ ?how much ?1-2litres" (058-035-143)"

(a) You have not adequately answered the question. Please identify the documentation from which you concluded that Adam: *"passed 200 mls of urine per hour"*.

This was an assumption based on his fluid intake and his known large volume of dilute urine and fact that fluid was not removed during dialysis.

(b) State whether you would have changed your anaesthetic management if Adam normally only passed urine at 50-70ml/hr and, if so, state how you would have changed it and for what reason. If you would not have changed your anaesthetic management, state why not.

If I had been certain that his urine output was fixed at 50-70 mls/hour then I would have administered 0.18NaCl/4%Glucose at this rate.

(110) Answer to Question 124(a) at p.46:

"0.18NaCl/4% Glucose is iso-osmolar with respect to plasma and is not isotonic as I stated. It has an osmolarity of 284 mosm/L compared to that of plasma 290 mosm/L."

(a) State whether you agree with the following proposition: 'All non-diabetic children maintain a normal plasma glucose concentration that varies very little (6-10 mmol/L) despite big fluctuations in glucose availability. This is due to the interplay of various hormones including insulin and glucagon. When glucose is infused into a child, then these hormones will act to maintain this plasma concentration at normal levels, by increasing peripheral utilisation and/or increasing glycogen storage.' If not, explain why not.

I agree with this proposition.

(b) State whether you agree with the following proposition: 'Although dextrose saline is isotonic and iso-osmolar with plasma in isolation (outside the body), once infused into blood the glucose in the solution diffuses out of the blood and is either taken up by peripheral tissue or is stored in the liver as glycogen, mainly under the influence of insulin.' If not, explain why not.

I agree with this proposition.

(c) State whether you agree with the following proposition: 'If the glucose in the dextrose saline solution disappears from the blood (by whatever mechanism), that means that what is left is 0.18% saline.' If not, explain why not.

I agree with this proposition.

(d) State what you think would be the result of infusing a large volume of 0.18% saline (no glucose) into a child.

In a child with normal renal function this could cause the serum sodium to fall depending on the urine loss and other fluids administered. In Adam's case this fluid was being used to provide maintenance fluid and to replace the additional on-going losses due to his large urine output.

(111) Answer to Question 126(b) at p.46:

"Prior to 26th November 1995 I would estimate I anaesthetised 15-20 children per week"

(a) Please describe your experience, prior to 26th November 1995, of anaesthetising children involved in operations where Mr Keane was (i) lead surgeon, (ii) assistant surgeon.

I believe that I had worked with Mr. Keane previously when a junior anaesthetist. I do not recollect whether he had been a lead or assistant surgeon.

(112) Answer to Question 126(c) at p.47:

"Prior to 26th November 1995 I do not have records of each renal transplant, nor their ages"

(a) You have not adequately answered the question. Please describe your experience, prior to 26th November 1995, involving children undergoing renal transplants, including the nature of your involvement.

I have no records detailing my experience with renal transplants in children. I did not provide anaesthesia for a renal transplant as a consultant prior to 1995. I had worked in RBHSC as a trainee in 1987 and as a Fellow in the Hospital for Sick Children, Toronto 1988-1990. I did participate in renal transplants and would have been supervised by a senior doctor.

(b) Describe your experience, prior to 26th November 1995, in assessing and managing fluids and electrolyte requirements in a child with renal failure.

As in (a) but also in my PICU role I would have managed such patients in the postoperative period. I have no detailed records of these patients.

(113) Answer to Question 128(c) at p.47:

"24.12.91 Laparotomy (050-023-071). Fluids administered; 5% Dextrose and Hartmanns boluses (x5). Anaesthetic record (049-009-019)"

(a) Please confirm if you were also involved in an operation on 25th December 1991 (Ref: 049-013-024)

No, the date on this anaesthetic record (049-013-025) is 20.12.91. (Ap pendix 3, Listing of RBHSC Admissions and Surgical Procedures)

(b) On 24th December 1991, Adam's pre-operative sodium was 128mmol/L (Ref: 050-024-171)

(i) State if you were aware of this result at the beginning of the operation on 24th December 1991. If you were not aware of this, explain why.

(ii) If you were aware of this result, state what actions you took (if any) to correct this sodium level. If you did not do anything, explain why.

(iii) State what you understood about the management of Adam's sodium level arising out of this procedure and whether you considered this in your plan for Adam's transplant surgery on 27th November 1995.

I cannot determine whether the sample was preoperative, or whether the result was available before, during, or more likely after the operation. The anaesthetic records do not give any indication of action on the basis of a Na result of 128.

(c) On 25th December 1991, Adam's pre-operative sodium was 127mmol/L. (Ref: 050-024-165)

(i) Explain why Adam's serum sodium result was 127mmol/L.

(ii) State if you were aware of this result at the beginning of the operation on 25th

December 1991. If you were not aware of this, explain why.

(iii) If you were aware of this result, state what actions you took (if any) to correct this sodium level. If you did not do anything, explain why.

(iv) State what you understood about the management of Adam's sodium level arising out of this procedure and whether you considered this in your plan for Adam's transplant surgery on 27th November 1995.

The sodium result of 127 on 25.12 91 was not a pre-operative result. There was no surgery on 25.12.91 (see 113a) and I was not involved in Adam's care on that date as he was back under Nephrology care.

(d) Following Adam's operation on 24th December 1991, you prescribed 4 ml/kg/h of 5% dextrose as his only postoperative fluid (Ref: 049-009-020). State whether this is a regime that you still follow, or whether you have changed your practice. Explain the reasons for your decisions.

I no longer use this regime because practice and knowledge has changed over the intervening period.

(114) Answer to Question 128(e) at p.48:

"[Lessons learned from Adam's death] To improve my documentation of fluid calculations and administration to children undergoing anaesthesia. Following Adam's death there has been improved reliability for testing of electrolytes in the operating theatre which assists with the monitoring of fluid and electrolyte administration."

(a) Describe and explain the improvements *"for testing of electrolytes in the operating theatre"* that you contend followed Adam's death.

An AVL analyser was bought to replace the IL machine. This together with using heparin crystals instead of liquid heparin provided more reliable and accurate sodium and potassium levels.

(b) State when those claimed improvements were instituted.

I do not recollect when the improvements occurred.

(c) Identify any protocol, guidelines or other document(s) reflecting those claimed improvements.

I cannot identify any such document.

(115) Answer to Question 129 at p.48:

"[Protocols and/or Guidelines which governed Adam's renal transplant surgery] Renal Transplantation in Small Children"

(a) Describe and explain the extent to which you consider that Adam's renal transplant complied with the governing protocol *"Renal Transplantation in Small Children"*.

Adam was an unusual case because he had native kidneys that produced large volume of dilute urine and he could not concentrate his urine in response to ADH.

(b) State whether you were aware of any application by the RBHSC to be an accredited institution with the King's Fund Organisation Audit (KFOA) Programme and standards in 1995. If so, state whether you believe the care and treatment of Adam complied with the KFOA standards, and explain the basis for your belief. If not, explain the respects in which it did not comply.

I was not aware of any application to KFOA in 1995

(c) If so, state whether you believe you complied with the KFOA standards in your care and

treatment of Adam.

II. ADDITIONAL QUERIES

(116) **In your PSNI Interview (Ref: 093-038-260) you state *"the benefit of being anaesthetised and sleepy it offers brain protection."***

(a) Explain the basis of your statement that *"the benefit of being anaesthetised and sleepy it offers brain protection."*

Control of oxygenation and carbon dioxide levels in the blood provide for brain protection after injury. During sedation or anaesthesia there is no coughing or straining that are known causes of raised intracranial pressure. These were the main treatment for closed head injury in the PICU at that time. That is why I suggested that there was an element of protection for Adam's brain during anaesthesia. *(Textbook of Pediatric Intensive Care, Rogers M. 1987 p 656)*

(b) Provide any clinical literature showing that anaesthesia has a protective effect on the brain when brain dysfunction is caused by a changing serum sodium

Hyponatraemia can lead to seizures. From Rogers chapter 19, "numerous authors have recommended the use of general anaesthesia ..... to minimize the metabolic sequelae of prolonged seizure activity or to suppress the process permanently". *(Textbook of Pediatric Intensive Care, Rogers M. 1987 p 627)*

(117) **Was the hazard notice HC (Hazard) (89) 31 'Blood Gas Measuring: The need for reliability of results produced in extra laboratory areas' brought to your attention, and if so when, by whom, in what circumstances:**

(a) State what action, if any, was taken by you as a result of this hazard notice and when was this action taken.

I cannot comment as I was in Toronto from June 1988-June 1990

(b) State what action, if any, was taken by others as a result of this hazard notice and when was this action taken.

I do not know what action was taken by others.

(c) If no action was taken, explain the reasons why not.

N/A

(d) State whether there was a written operational protocol for the blood gas analyser machine used on 27th November 1995 at approximately 09.32, and if so, state whether it was available to the user and was attached to the machine. If there was no written operational protocol, state the reasons why not. If there was a written operational protocol but it was either not available to the user, or was not attached to the machine, state the reasons why not.

I do not know if there was a written protocol.

(e) State what steps were taken by RBHSC prior to 27th November 1995 to ensure that the results of the blood gas analyser machine used at 09.32 in relation to Adam were comparable with those produced by a quality-controlled laboratory-based instrument.

I do not know.

(118) **State whether you were aware of any discussions relating to Adam's death and his inquest involving the Trust, clinical or managerial staff concerning the lessons that could be learned and/or action that should be taken.**

(a) If so, state when those discussions took place, who participated in them and what the outcome was.

Dr Gaston managed this.

(b) State, in particular, the extent to which you were involved in any such discussions and/or action.

I was involved in producing the draft statement.

(c) If you were not involved in either discussions or action, explain why not.

(119) **State whether you were required to (i) formally report Adam's death and the circumstances thereof and/or (ii) explain what happened to Adam to a senior manager or clinician within the Trust. If so, state:**

(a) to whom and when you reported/explained this

I reported to Dr Gaston and Dr Murnaghan in relation to the Inquest following Adam's death.

(b) the nature of the report/explanation

Deposition to the Coroner.

(c) the outcome thereof

Attendance at the Coroner's Inquest.

(d) any document relevant thereto.

Coroner's additions to my Deposition.

(e) If you did not report/explain this, explain why not.

(120) **Describe the procedure for clinical audit at RBHSC in November 1995 and identify any relevant documents**

(a) Describe the <u>current</u> procedure for clinical audit at RBHSC and identify any relevant documents

In RBHSC there are monthly meetings. Deaths are presented and discussed. Following this there are a number of audit presentations.

(b) Describe what you did in terms of a 'clinical audit' of Adam's case, and provide any relevant documents

I did not do anything in terms of clinical audit as it was a Coroners Inquest.

(c) State whether your actions relating to a clinical audit of Adam's case would differ in 2011 and if so, state how. If not, explain why not.

I do not think my actions would be different in 2011.

(121) **Describe the procedure for discussions of deaths amongst medical personnel (e.g. 'death**

meetings' / 'morbidity and mortality meetings') at RBHSC in November 1995 and identify any relevant documents

(a) Describe the current procedure for discussions of deaths amongst medical personnel (e.g. 'death meetings' / 'morbidity and mortality meetings') at RBHSC and identify any relevant documents

In RBHSC there are monthly meetings. Deaths are presented and discussed. Following this there are a number of audit presentations.

(b) Describe whether you participated in any such meetings in Adam's case, and if so, state when and provide any relevant documents

Yes the case would have been discussed at the Paediatric Audit meeting the month after the death but the Minutes are not still available.

(122) State your involvement, if any, at any stage with the clinical negligence claim which was pursued following Adam's death.

No Involvement

(123) Attached is a table showing the various phases in Adam's renal transplant operation. Using the initials of each person or, in the event of not knowing the identity of the person, the job title, state under each phase the personnel who were:

(a) present using the "+" symbol and

(b) actively participating using the "++" symbol.

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

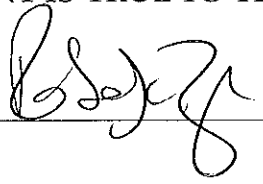
Signed:  **Dated:** 28/9/u

TABLE FOR PAEDIATRIC RENAL TRANSPLANT
Showing the involvement of personnel in the various phases

Phase of the transplant process	Physicians/ ward staff/ ICU staff	Anaesthetists	ODA/ ODP/ MTO	Surgeons	Scrub nurse	Runner
1. Transplant option first mentioned to family	?MS++					
2. Transplant surgery consent process started; risks/benefits explained	?MS++					
3. Preoperative preparation on evening of admission; consent confirmed	?MS++					
4. Preoperative preparation; fasting, i.v. fluids; blood tests; dialysis; ultra sound of neck re: CVP line	Trainee++	TM++				
5. Preparing theatre for start of surgery/check monitors & equipment		RT++ TM++ Nurse++	PS++		Nurse++	Aux Nurse++
6. Preparing donor kidney				PK++	Nurse++	Aux Nurse++
7. Patient arrival in operating theatre; i.v. inserted; anaesthesia induced		RT++ TM++ Nurse++	PS++		Nurse++	Aux Nurse++
8. Insertion epidural, arterial and CVP lines; x-ray of the CVP line and uretheral catheter inserted		RT++ TM++ Nurse++	PS++		Nurse++	Aux Nurse++
9. Pre-transplant phase of surgery	MO'C++	RT++ TM++ Nurse++	PS++	PK++ SB++	Nurse++	Aux Nurse++
10. Vascular and ureteric anastomoses performed; ureteric and/or suprapubic catheter inserted		RT++ Trainee++ Nurse++	PS++	PK++ SB++	Nurse++	Aux Nurse++
11. Post-transplant phase of surgery including wound closure		RT++ Trainee++ Nurse++	PS++	PK++ SB++	Nurse++	Aux Nurse++

12. Post-surgery; anaesthesia stopped; drapes removed; drains connected		RT++ Trainee++ Nurse++	PS++	SB++	Nurse++	Aux Nurse++
13. Child transferred to ICU		RT++ Trainee++ Nurse++	PS++			
14. Communicating child's condition at end of surgery to parents	MS++	RT++				
15. Communicating child's death to parents	MS++ PICU Nurse++					

Dr. R. Taylor WS008/4 Revised answer to Q54a,b,c,d.

54 Answer to Question 37(a) at p.18:

"I cannot remember who [I worked with to determine the cause of Adam's death]. It would have been with the nephrologists and anaesthetists in PICU."

(a) **State whether you were present during Adam's autopsy and if so: (i) for how long you were present; (ii) the circumstances in which you came to be there; (iii) exactly what was discussed between yourself and Dr. Alison Armour, the pathologist.**

I do not remember being present at his autopsy.

(b) **State whether it was you who filled in Adam's autopsy request form (copy attached, Ref: INQ-0343-11). If not, state who filled in this document.**

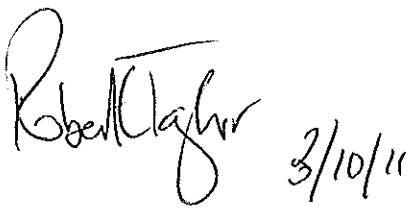
Yes I filled in the Autopsy request form.

(c) **If you did fill in the autopsy request form, explain what you meant by *"osmotic disequilibrium syndrome"*. State if you still consider this to have been a possible cause of Adam's death. If so, explain your reasons why. If not, explain why.**

The words "osmotic dysequilibrium syndrome" were Dr Webb's (058-035-140).

(d) **Explain what you meant by Adam being *"a somewhat bizarre case of a child undergoing renal transplantation"* and explain the basis on which you formed that view.**

I considered it an odd case in that I could not explain the findings on the basis of the Clinical Presentation I recorded on the Autopsy Request Form.



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BRIEF REPORT

A fatal case of cerebral oedema with hyponatraemia and massive polyuria after renal transplantation

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Abstract We report the case of a child who died from severe cerebral oedema in the context of hyponatraemia and extreme polyuria immediately after renal transplantation. The patient was treated according to a standard post-transplantation protocol, receiving 0.45% saline solution for urine output replacement. The case highlights the dangers of massive fluid therapy in the context of polyuria and, therefore, the need for intensive monitoring.

Keywords Hyponatraemia · Seizure · Cerebral oedema · Kidney transplant · Hypotonic fluid · Polyuria · Salt wasting

Introduction

We report the case of an 11-year-old boy, who had extreme polyuria shortly after live-related renal transplantation. He developed seizures associated with a serum sodium concentration of 126 mmol/l and his condition rapidly progressed to tonsillar herniation and death. We detail the sequence of events, discuss potential causes of this tragic occurrence and describe how we changed our post-transplantation care protocol to enable earlier detection of such abnormalities.

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Case report

An 11-year-old boy weighing 30.3 kg was admitted for a pre-emptive live-related transplant. He had suffered meningococcal septicaemia at the age of 34 months, complicated at that time by severe neurological dysfunction, with coma, seizures and peripheral vascular involvement with skin and bone loss. He had been undergoing short-term dialysis for nearly 4 weeks, but his renal function [glomerular filtration rate (GFR) by the chromium-51–ethylene diamine tetra-acetic acid (Cr^{51}-EDTA) method was 37 ml/min per 1.73 m^2 body surface area at 3 years] had recovered sufficiently to be managed conservatively. He was left with a minor seizure disorder treated with sodium valproate at the time of transplantation. Electroencephalography (EEG) showed discharges over the right temporoparietal area, and a cerebral magnetic resonance imaging (MRI) scan when he was aged 4.5 years showed mild cerebellar atrophy, with normal ventricular size. He attended mainstream school and had learning support.

His renal function deteriorated from the age of 10 years, with his serum creatinine rising from 1.6 mg/dl to 3.8 mg/dl (145–330 μmol/l), so work-up was commenced for renal transplantation. He was polyuric, with a daily urine output of 3–4 l.

He underwent a live-related renal transplantation, with 0,1,1 mismatch, from his mother. He was given 0.25 mg/kg tacrolimus and prednisolone 600 mg/m^2 before theatre and had a urethral catheter placed after being anaesthetised. The operation was uneventful; the patient had normal vessel

anatomy. There was good blood flow and immediate urine output. The cold-ischaemia time was 30 min, and anastomosis time was 25 min. Intraoperatively, his systolic blood pressure (SBP) was 100-130 mmHg and central venous pressure (CVP) was 10-15 cmH_2O. He was given a total of 2,200 ml of fluid during the procedure [1,000 ml Hartmann's solution (near isotonic sodium lactate) and 1,200 ml 4.5% albumin] and 60 mg furosemide. A dopamine infusion (3 μg/kg per minute) and a patient-controlled morphine infusion were commenced. He received routine immunosuppression with tacrolimus, azathioprine and prednisolone.

Immediately postoperatively, he was warm and well perfused, with a core–toe temperature gap of 2.4°C. He had a normal heart rate (HR; 90-105 beats/min) but was hypertensive (SBP 130-140 mmHg). His CVP was 8-11 cmH_2O. He regained consciousness fully and was extubated, with saturations of 98–100% in room air, respiratory rate 25/min. He had mixed metabolic and respiratory acidosis, pH 7.25, with a carbon dioxide partial pressure (pCO_2) of 42 mmHg (5.6 kPa) (venous gas). His initial postoperative serum sodium level was 141 mmol/l (see Table 1). A bedside fluid balance sheet was established, which included the volume of urine in the catheter bag (1,180 ml) but not the fluids given in theatre (2,200 ml) or the undocumented losses (urine lost during anastomosis of the ureter to the bladder, and blood losses). These losses were retrospectively estimated by the surgeon to be 300–500 ml.

The patient developed massive polyuria almost immediately after anastomosis, passing urine up to 58 ml/kg per hour. He was treated according to the unit's protocol, with replacement of insensible losses of 400 ml/m^2 per day and of the previous hour's urine volume with the same volume of 0.45% saline solution, alternating with 0.45% saline solution/2.5% dextrose. Two hours postoperatively he developed signs of poor peripheral perfusion, with a core–toe temperature gap of 6°C; HR was 90–105 beats/min, and SBP was 130–150 mmHg. It was concluded that he had a fluid deficit, and he was given an extra 1,449 ml 0.9% saline solution over 2 h. At 4 h he had a generalised tonic–clonic seizure, which was terminated immediately following administration of 0.1 mg/kg lorazepam. Blood glucose measured with a stix was 8.6 mmol/l, and central venous gas showed uncompensated metabolic acidosis, with a pH of 7.1. He was hyponatraemic (126 mmol/l), initially thought to be an artefact but confirmed on a repeat sample (121 mmol/l). At 5 h he had a further generalised tonic–clonic seizure, which again responded to lorazepam, but at that time his pupils were fixed and dilated. He was

Table 1 Results of blood and urine tests and fluid balance

Parameter	Time after anastomosis								
	Preoperative	Postoperative	1 h	2 h	3 h	4 h Seizure	5 h Seizure	Normal range	Unit
Sodium	140	141				126	121	133–146	mmol/l
Total CO_2	22	18				15	17	20–30	mmol/l
Urea	97 (34.5)	76 (27.2)				38 (13.7)	33 (11.7)	7–17 (2.5–6.0)	mg/dl (mmol per litre)
Creatinine	6.0 (528)	4.3 (379)				2.0 (178)	1.6 (143)	0.4–0.9 (35–80)	mg/dl (μmol/l)
Total calcium	11.3 (2.81)	9.7 (2.42)				6.8 (1.7)	6.5 (1.61)	8.8–10.7 (2.19–2.66)	mg/dl (mmol/l)
Magnesium	1.9 (0.8)	2.0 (0.83)				0.9 (0.36)	0.7 (0.28)	1.7–2.3 (0.7–0.95)	mg/dl (mmol/l)
Albumin	42	51				41	37	37–56	g/l
Glucose		202 (11.2)				175 (9.7)		63–99 (3.5–5.5)	mg/dl (mmol/l)
Osmolality								270–285	mosmol/kg
Haemoglobin	11.6	9.3				8.6		11.5–15.5	g/dl
Urine									
Sodium	112								mmol/l
Osmolality									mosmol/kg
Fluids									
In		2,200[a]	1,303	1,485	2,383	2,591	1,898		ml
Out[b]		1,240[c]	1,170	1,760	1,740	1,620	1,150		ml
Cumulative Balance		+960	+1,093	+818	+1,461	+2,432	+3,180		ml

[a] Total amount of fluid given intra-operatively
[b] Except for 200 ml from the wound drain, all output was urine
[c] Immediate postoperative output did not include intra-operative losses, which were not documented (see text)

intubated and ventilated; a computed tomography scan revealed severe cerebral oedema, with uncal and tonsillar herniation; he was diagnosed as being brainstem dead the following morning. Using hypertonic (3%) saline solution, we achieved normonatraemia after 8 h to allow organ donation.

Discussion

Our case highlights the dangers of massive fluid therapy and biochemical disturbances in the face of extreme polyuria. There are obvious questions regarding the aetiology of the patient's seizures, hyponatraemia and polyuria. Moreover, considering that the patient was treated according to a standard protocol, used for over 15 years in more than 200 paediatric renal transplantations, we describe how the protocol was changed in order to prevent a similar tragedy from occurring.

What caused the patient's seizures and subsequent tonsillar herniation?

Seizures are a recognised complication after renal transplantation, with a frequency of up to 24%, with potential causes including fluid overload, and corticosteroid and calcineurin-inhibitor therapy [1–3]. Our patient was known to have had seizures previously, indicating that he had a lowered seizure threshold which was reduced further by the hypocalcaemia and hypomagnesaemia after transplantation (Table 1). The first seizure in our patient occurred when the serum sodium level was 126 mmol/l, a level not usually associated with seizure activity. However, hypo-osmolality was likely to have been the key aetiological factor, as the drop in serum sodium level was compounded by the rapid fall in urea after transplantation. His calculated serum osmolality dropped by approximately 80 mosmol/kg between transplantation and first seizure.

Why was the patient polyuric?

The massive diuresis after anastomosis (58 ml/kg per hour) was extremely unusual. There is one report of an adult with diuresis of 25–50 ml/kg per hour after having received a live-unrelated renal transplant, who was also given fluid replacement with 0.45% saline solution and who developed hyponatraemia [lowest serum sodium (Na) concentration 113 mmol/l] and multiple generalised tonic–clonic seizures [4].

Our patient had 3–4 l/day (4–5 ml/kg per hour) native urine output, and the massive fluid losses after transplantation would have included a proportion from the native kidneys. However, excretion of ~1,800 ml/h requires a GFR of at least 30 ml/min, whilst the estimated GFR in our patient was 6 ml/min, uncorrected for surface area. Therefore, the majority of urine must have derived from the graft. Glucose given in the replacement fluid caused mild hyperglycaemia, with levels of 10–11 mmol/l, leading to osmotic diuresis. However, this leads to free water losses and hypernatraemia and is, thus, probably less relevant here.

Why did the patient become hyponatraemic?

The patient's venous sodium level had dropped from 141 mmol/l post-operatively to 121 mmol/l 5 h later. Hyponatraemia is due to either a deficiency in salt or an excess of water.

A separate quantitative analysis of water and salt balance, also called tonicity balance, can help identify the pathophysiology of hyponatraemia [5]. From the beginning of surgery till his death, the patient was given 11.8 l and lost 8.6 l (see Table 1), a net positive balance for water of 3.2 l. An expansion of his total body water (estimated at 20 l or 65% of body weight) by this amount is consistent with the observed dilution of his serum sodium from 141 mmol/l to 121 mmol/l ($141 \times 20/23.2 = 121.6$). Based on this first part of the tonicity balance, excess fluid accounted for the hyponatraemia. This fits also with the observed decrease of albumin and haemoglobin in the blood (see Table 1). However, in order to retain the extra 3.2 l as free water, he must have been in equal sodium balance, i.e. the amount of sodium lost in the urine must have been equal to the sodium received. Whilst the urinary sodium was not measured, the amount received can be calculated from the fluids administered, and it totalled 1,140 mmol. An excretion of 1,140 mmol sodium in 8.6 l of urine equates to 133 mmol/l and represents 20% of sodium filtered during that time (assuming a GFR of 100 ml/min), indicating sodium wasting. This compares to reports of fractional sodium excretion (FE_{Na}) as high as 46% in deceased-donor renal allografts on the day of transplantation [6].

Why did the patient have sodium wasting?

Sodium wasting is likely to have been due to hypoxic–ischaemic injury to the graft. The high FE_{Na} reported in deceased-donor allografts was associated with ischaemic changes on biopsy [6]. In another study, hyponatraemia was seen in 88 of 125 adult recipients, also associated with an increased FE_{Na} [7]. The dramatic postoperative decrease of serum calcium and magnesium concentrations (Table 1), which clearly exceeded the 16% dilution explained by the fluid balance, also suggests tubular dysfunction.

Sodium wasting can also be an appropriate physiological response of the kidney to volume overload, but it should not lead to hyponatraemia, as water can be excreted

alongside. However, other factors could have led to water retention, such as stress and morphine, recognised non-osmotic stimuli for antidiuretic hormone [8], or furosemide, which impairs urinary dilution.

How should a polyuric patient be treated?

For a patient with gross polyuria (> 10 ml/kg per hour) we suggest giving a fixed intake of 10 ml/kg per hour, with frequent (two-hourly) clinical and biochemical assessments that include blood pressure, peripheral perfusion, CVP, and serum and urine sodium and osmolality, to guide further replacement. We use 0.45% saline solution, based on our subsequent experience with typical post-transplantation urinary sodium concentrations of approximately 80 mmol/l. Any extra fluid for perceived volume depletion must be given in isotonic form. We use a glucose-containing solution at a steady rate for replacement of insensible losses, but fluids given for urine output replacement and boluses are glucose-free.

Conclusion

Our patient developed seizures and tonsillar herniation due to hypo-osmolality associated with the administration of large volumes of hypotonic intravenous fluids in the context of extreme polyuria. Other factors, such as his previous brain injury, might have contributed to the fatal outcome. Regardless, the case highlights the importance of close clinical and biochemical monitoring after transplantation, especially in the context of polyuria. Although, in this case, the rapidity of events suggests that these measures might not have prevented death, we hope that lessons from this case will help to modify practice and prevent future tragedies.

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Fasting in children for day case surgery

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Key words: PREOPERATIVE; HYPOGLYCAEMIA; CHILDREN; DAY CASE

Summary

Thirty-four children admitted for day case surgery were studied to determine the period of preoperative fasting and blood sugar concentrations at the time of induction of anaesthesia.

Of these, 88% fasted for 12 h or more, 20% fasted for 16 h or more. Three were found to be hypoglycaemic.

The introduction of routine 'mid-day' operating lists for paediatric day case surgery is suggested as a method of reducing the period of fasting and risk of hypoglycaemia.

Introduction

Day case surgery is increasing. Children requiring short procedures such as insertion of grommets are particularly suitable for this as they recover rapidly and there are few postoperative complications.

Since the early 1970s several studies have been undertaken to determine the optimal period of preoperative fasting. Anaesthetists generally feel that adequate preoperative fasting is essential for gastric emptying and to minimise the risk of regurgitation of stomach contents at the time of induction of anaesthesia *(1)*. A period of 4–6 h is accepted as adequate. However, a number of authors have noted that a minority of young children become hypoglycaemic by the time of induction of anaesthesia *(2)*. Hypoglycaemia reduces cerebral tolerance to hypoxaemia and hypotension. Young children may not tolerate fasting as well as adults as they have a relatively higher obligative glucose requirement *(3)*. Thomas *(4)* found 28% of children less than 4 years of age and 15.5 kg were severely hypoglycaemic at the time of induction of anaesthesia. This finding has not generally been confirmed.

The aim of this study is to determine the actual period of preoperative fasting in children admitted to our day care unit and to assess their blood sugar levels at the time of induction of anaesthesia.

Routinely, all patients to be admitted to the day care unit are advised to fast from 12 midnight on the eve of admission, until after the operation.

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Patients and methods

A total of 34 consecutive children admitted to the day care unit aged between 11 months and 99 months for insertion of grommets were studied. The age and weight of each child was recorded preoperatively, together with the *actual* period of fasting. This was assessed by enquiring from a parent the time that food or drink was last taken and recording the time of induction of anaesthesia. After induction, blood was taken from the antecubital vein for laboratory analysis of glucose concentration by the glucose oxidase method. Patients had no known illness (except surgical indication) and were suitable for day case surgery in accordance with the guidelines of the Royal College of Surgeons (1985).

Each had grommets inserted, a procedure which takes approximately 10 min.

Results

The age, weight, period of fasting and blood sugar level at the time of induction of anaesthesia, together with the mean, standard deviation and range for each is recorded in Table I.

Two aspects of these results were further analysed and are reported below.

PERIOD OF PREOPERATIVE FASTING

The period of preoperative fasting was in all cases much longer than that required for gastric emptying. The mean preoperative fasting time was 14 h (SD=1.9 h); 88% of children fasted ≥12 h, 20% fasted ≥16 h.

BLOOD SUGAR CONCENTRATIONS (AT INDUCTION)

In three of 34 cases (8.8%) the blood sugar level was found to be less than 3.0 mmol/l (2.3, 2.7 and 2.9 mmol/l).

TABLE I *Summary of results*

Parameter	*Mean*	*SD*	*Range*
Age (months)	59	24	(11–99)
Weight (kg)	18.4	4.25	(10.8–25.2)
Blood sugar (mmol/l)	4.16	0.63	(2.3–5.4)
Fasting (h)	14	1.88	(9.5–17)

No child showed any clinical evidence of hypoglycaemia. All other patients had levels in the normal laboratory range (3.3–5.6 mmol/l).

The relationship between age and blood sugar, weight and blood sugar, and fasting time and blood sugar was assessed. No simple indicator could be found to predict which cases would have a low blood sugar at the time of induction.

Discussion

FASTING PERIOD

The most remarkable result of this study was the prolonged period of preoperative fasting to which these children were subjected. This arose partly because 'standard' advice was given to parents (namely 'Nothing to eat or drink from midnight') and failing to take into account the age and daily routines of these children.

Since many young children eat their last meal of the day in the early evening (say 7 pm) and then go to bed, they will already have starved for 5 h before midnight. Our day case operating sessions start at 8.30 am, therefore the first child on the list will have fasted for 13.5 h. Children late on the list will have fasted for longer periods.

The period of fasting in this study was recorded until the time of induction of anaesthesia. There is, therefore, a further period of fasting during the operation and until recovery from the anaesthetic permits an oral intake. During the operative period a rise in the blood sugar concentration is typical, probably a stress related adrenergic response. However, a fall in blood sugar concentration has been documented in some children. The period of time between induction of anaesthesia and first oral fluids is not usually prolonged—typically 1–3 h in our experience. Payne and Ireland *(5)* measured a mean of 3 h and a range of 1–7 h in their study.

HYPOGLYCAEMIA

When comparing the various studies on this subject one must look at the definition of hypoglycaemia used. Various levels have been accepted by different authors.

Allison *(3)* suggested a grading system—less than 3.3 mmol/l=mild; less than 2.8 mmol/l=moderate and less than 2.2 mmol/l=severe. This system is helpful as some children may be symptomatic at levels above 2.2 mmol/l *(6)*.

In this study we found one case of mild and two cases of moderate hypoglycaemia. In common with other authors except Thomas *(4)* and Welborn *et al. (7)* we could find no simple predicting factor in terms of age, weight or period of starvation. In both the Thomas and Welborn *et al.* studies the children were planned for afternoon surgery. Welborn *et al.* found two children who became hypoglycaemic after a period of 17 and 19 h fasting respectively. All other studies have been based on morning operating sessions and a diurnal variation in glucose utilisation may account for the difference found.

Hypoglycaemia during anaesthesia is not without risk, and case reports of hypoglycaemia-induced seizures have been recorded *(8)*.

MANAGEMENT

Various methods have been suggested to satisfy the requirement of preoperative fasting and to avoid the risk of hypoglycaemia. Many authors have suggested feeding either milk or glucose solutions in proportion to the child's weight 4 h preoperatively. On a day case basis this would involve waking a child at 4.30 am to feed. This is naturally disruptive and a substantial number of children, 29% in one study *(9)*, refused the feed in the middle of the night. In those children who accept a feed at this time 4–6 h preoperatively there is a significantly raised blood sugar concentration only in those *over* 4 years of age *(9)*. Some authors have suggested the use of glucose solutions intravenously during the anaesthetic. There is a significant rise in blood sugar concentrations in these cases.

Management of these children in the preoperative period remains contentious with widely differing advice being given in the various centres referred to in this account.

Overnight fasting leads to excessively long periods of abstinence which, if not hazardous, are undesirable. Feeding in the middle of the night is disruptive and may be refused.

One possible solution would be the introduction of 'mid-day' lists for day case surgery starting at 11 am and ending at 1 pm. This would allow a light breakfast to be taken at 7 am with little inconvenience. No child would fast preoperatively for more than 6 h, reducing the risk of hypoglycaemia and leaving ample time for postoperative recovery.

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HYPOGLYCAEMIA IN CHILDREN BEFORE OPERATION: ITS INCIDENCE AND PREVENTION

D. K. M. THOMAS

SUMMARY

Two groups of children, comparable in age and weight were studied. The first, the Starvation Group (SG), underwent normal preoperative starvation. The second, the Milk Group (MG), received milk orally 4 hours prior to operation. At operation the mean blood glucose concentration was 53.3 mg/100 ml in the SG and 66.4 mg/100 ml in the MG. The difference between the two groups was statistically significant. Hypoglycaemia occurred only in those children in the SG who were less than 47 months of age and 15.5 kg body weight.

The mean normal fasting blood glucose concentration at birth is 54 mg/100 ml with a range of 28–96 mg/100 ml (Bowie, Mulligan and Schwartz, 1963). The concentration increases in childhood to a mean of 77 mg/100 ml at 2 years and 92 mg/100 ml at 15 years (Mayer, 1951).

After the third day of life hypoglycaemia is defined as a blood glucose concentration of less than 40 mg/100 ml (Cornblath and Schwartz, 1966; Habbick, McNeish and Stephenson, 1971). This level has been accepted for this study although other authors have suggested higher limits of 50 mg/100 ml (Ehrlich, 1971) and 60 mg/100 ml (Bowie, Mulligan and Schwartz, 1963). Hypoglycaemia is provoked by fasting, although it is not an inevitable consequence of withholding food. The body conserves glucose by a decrease in the concentration of circulating insulin and an increase in the concentration of growth hormone (Glick et al., 1965). The concentrations of circulating growth hormone, glucagon, cortisol and adrenaline are increased by a fall in blood glucose concentration to hypoglycaemic levels (Marks and Rose, 1965). Hypoglycaemia is not a disease but is a clinical sign (Conn and Seltzer, 1955). In a study of blood glucose concentrations in children prior to surgery it was found that 10% of the children had a blood glucose concentration in the hypoglycaemic range (Watson, 1972). Blood glucose concentrations less than 60 mg/100 ml were found in 30% of starved children at the time of induction of anaesthesia (Bevan and Burn, 1973).

This study was designed to compare blood glucose levels in two groups of children and to assess the influence of preoperative feeding on the frequency of hypoglycaemia.

METHOD

The children were all admitted to the same ward the day before operation. The operations occurred between 1400 and 1600 hours and were for the correction of strabismus. After an overnight fast they received a bowl of cereal and a drink of milk at 0600 hours.

The children were in the weight range 9–36 kg and were aged between 19 and 166 months. They were divided into two groups. The first group (31) received no further food prior to operation. The second group (29) were given a drink of milk, 10 ml/kg body weight, up to a maximum of 300 ml, 4 hours before operation.

All the children were given trimeprazine 1.7 mg/kg body weight (maximum 30 mg) orally 4 hours before operation. Morphine 0.25 mg/kg and atropine 0.02 mg/kg were given by intramuscular injection 1 hour before operation. Anaesthesia was induced with thiopentone 4 mg/kg followed by pancuronium 0.13 mg/kg given intravenously. The lungs were ventilated with oxygen and nitrous oxide from a facepiece until an oral endotracheal tube could be passed. Ventilation was continued manually with oxygen 30% in nitrous oxide using a modified T-piece system. A Ryle's tube was passed into the stomach and the contents were aspirated. After the removal of the tube a mouth pack was inserted. Two minutes after endotracheal intubation 2 ml of blood were taken from the long saphenous vein and stored in a fluoride bottle. The blood glucose concentrations were measured by the autoanalyser method of

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...ley, Dawson and Marks (1968). This method ...an accuracy of ±5%.

At the end of the operation the neuromuscular ... was reversed with atropine (0.02 mg/kg) and ...stigmine (0.07 mg/kg) injected intravenously. ...e mouth pack was removed and the children were ...ated while lying on their sides.

There was no vomiting or regurgitation in either ...up during induction of anaesthesia, operation or ...overy.

The volume of the aspirated stomach contents ...measured and the pH measured by a dipstick ...thod.

RESULTS

...bles I and II show the ages and weights of the ...dren. There was no significant difference between ...two groups.

...In the SG the mean blood glucose concentration ...53.3 mg/100 ml (SD 16.1). The MG had a ...n blood glucose concentration of 66.4 mg/100 ml ...12.6) (table III). Using the Student *t*-test the ...rence between the means of the two groups was ...ificant (P<0.0005). 15.2% of the SG children ...ome of the MG children were hypoglycaemic ...blood glucose concentration less than 40 mg/ ...00 ml). The difference was significant (P=0.05).

...ll hypoglycaemia was observed only in the ...ger and smaller children in the SG, those older ...n 47 months and weighing more than 15.5 kg ...re excluded from further analysis (table IV). The ...ger children in the SG had a mean blood glu- ...e concentration of 46.4 mg/100 ml (SD 16.5). ...e mean for the MG was 60.0 mg/100 ml ...9.2) (table V). The difference between the two ...ups is significant (P<0.0005). 28% of the SG ...dren were hypoglycaemic (table VI).

The amount of stomach contents aspirated did ...exceed 15 ml in any child. The mean pH of the ...mach contents in the SG was 2.9 and in the ...MG 7.7 (table VII).

DISCUSSION

...e author's experience the duration of preopera- ...starvation in children undergoing operations in ...afternoon is 8–10 hours. For a morning opera- ...this period of starvation extends to more than ...ours. It has been stated that starvation does not ...ally lead to hypoglycaemia (Glick et al., 1965) ...this study has shown that 28% of children ...4 months old and 15.5 kg in weight were ...ypoglycemic in terms of the criteria of Cornblath

TABLE I. *Mean weight of the children.*

	Number	Mean weight (kg)	SD	Range (kg)
Starvation group	33	18.6	6.6	9–36
Milk group	29	20.0	6.4	11–35

TABLE II. *Mean age of the children.*

	Number	Mean age (months)	SD	Range (months)
Starvation group	33	59	30.9	23–141
Milk group	29	69	37.2	19–166

TABLE III. *Mean blood glucose levels.*

	Number	Mean blood glucose (mg/100ml)	SD	Range (mg/100ml)
Starvation group	33	53.3	16.1	10–80
Milk group	29	66.4	12.6	40–95

Difference significant (P<0.0005).

TABLE IV. *Incidence of hypoglycaemia in starvation group in relation to age and body weight.*

	Number	Hypo-glycaemic	Normal blood glucose conc.
Starvation group less than 47 months and 15.5 kg	18	5	13
Starvation group more than 47 months and 15.5 kg	15	0	15

TABLE V. *Mean blood glucose in children less than 47 months of age and 15.5 kg weight.*

	Number	Mean blood glucose (mg/100ml)	SD	Range (mg/100ml)
Starvation group	18	46.4*	16.5	10–65
Milk group	11	60.0*	9.2	40–70

*P<0.0005.

TABLE VI. *Incidence of hypoglycaemia in children less than 47 months in age and 15.5 kg in weight.*

	Number	Hypoglycaemic	%
Starvation group	18	5	28
Milk group	11	0	0

TABLE VII. *Mean volume of stomach contents and pH.*

	Number	Mean volume stomach contents (ml)	SD	pH
Starvation group	33	6.0	3.1	2.9
Milk group	29	8.0	2.8	2.7

and Schwartz (1966) and Habbick, McNeish and Stephenson (1971). The mean fasting blood glucose concentration in children is in the range 50–90 mg/100 ml (Baron, 1970) but this study showed a range from 10 to 80 mg/100 ml with a mean value very close to that for newborn infants.

Some children examined by the author before operation have shown signs that could be attributed to hypoglycaemia, including sweating, paleness of the skin and complaints of headache. Random blood glucose estimations using dextrostix had suggested that hypoglycaemia may have been present; this was a stimulus to the present study. In the present study none of the children with confirmed hypoglycaemia had clinical signs or symptoms of the condition. Nevertheless this study would suggest that starvation lasting 8 hours or more is excessive.

The MG showed no patient with hypoglycaemia and had a significantly greater mean value of blood glucose. In the present small series there was no vomiting or regurgitation. This would suggest that the administration of milk, 4 hours prior to anaesthesia, may be a safe and advantageous procedure if the same method of premedication and anaesthesia are followed. This is supported by the small volumes of stomach contents that were aspirated.

A study of the possible morbidity resulting from hypoglycaemia, due to preoperative starvation, would seem to be a useful field of study. It may be that the presence of hypoglycaemia is unde and that its prevention in a safe and simple n is an advantage.

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index. The lower limit of the therapeutic range is 5 mg/dl, and although eight of ten patients in this study had magnesium concentrations below this minimum therapeutic level, none of the levels was so low that fasciculations occurred.

The interactions of magnesium and neuromuscular blocking drugs have been previously studied. Morris and Giesecke[2,3] showed that the effects of *d*-tubocurarine and magnesium sulfate are additive and that *d*-tubocurarine is approximately a thousand times as potent as magnesium sulfate as a neuromuscular blocking agent. Aldrete *et al.*[4] gave healthy male surgical patients 1 g magnesium sulfate intravenously and found that this dose decreased the frequency and intensity of muscle fasciculations following the injection of succinylcholine, as well as preventing the rise in serum potassium that otherwise occurred.

The present study has demonstrated that succinylcholine-induced muscle fasciculations are extremely unlikely to occur in the toxemic patient who has received sufficient magnesium sulfate to increase her serum concentration of magnesium significantly above the upper limit of normal. These patients do not need pretreatment with *d*-tubocurarine before succinylcholine administration to prevent fasciculations.

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Hypoglycemia-induced Seizures in an Infant during Anesthesia

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Ketamine hydrochloride is a popular drug for producing immobility during radiation therapy in young children. In certain patients methohexital sodium, 5 per cent, given by deep intramuscular injection has also proven to be a useful agent for this purpose. We present a case in which convulsions occurred following treatment with methohexital sodium.

Report of a Case

A 4-month-old, 6.5-kg male infant had been diagnosed at 8 weeks of age as having a retinoblastoma. He underwent enucleation of the left eye, and radiation therapy to his right eye was begun. His first seven treatments were uneventful. For his eighth treatment an intramuscular injection of methohexital, 65 mg, was given into the anterior aspect of the thigh. Three minutes later the infant fell asleep and was placed on the radiation table for treatment. At that time his blood pressure was 80 torr and heart rate 120/min. Ten minutes after the injection of methohexital and at the end of the treatment, the child had a bilateral tonic clonic seizure, and it was noticed that his eyes rolled backwards. Heart rate was 120/min and blood pressure was 90 torr by palpation. Mild respiratory obstruction and central cyanosis were treated by the use of an oral airway and administration of oxygen by mask. A new bottle of Dextrostix® in which the Dextrostix strips all matched the "O" color block was obtained. The bottle had been stored at approximately 28–30 C. The Dextrostix analysis showed a blood glucose level of 25 mg/dl. The child was given dextrose, 25 per cent, 20 ml. The seizures, which had lasted about 5 min, stopped shortly after the infusion. Analysis of blood drawn at this time showed a calcium concentration of 10.2 mg/dl, normal electrolyte values, and no ketonemia. The temperature was 37 C. A lumbar puncture showed three cells, protein 27 mg/dl, and glucose 48 mg/dl. A blood glucose test performed an hour later showed 109 mg/dl. Within 30 min of the seizure the child was active and behaved normally. Two hours after the seizure the child ate without incident. On further inquiry, it was determined that the mother usually fed the child at about 2 AM each night, but on the evening before therapy the child had slept from 6 PM until just prior to their arrival at the hospital. Hence, the mother had not fed the child for nearly 13 hours. The child subsequently underwent further radiation therapy without problems. Blood glucose levels were periodically checked and found to be normal. To rule out latent epilepsy, an electroencephalogram (EEG) was performed; it disclosed no abnormality. Methohexital sodium, 65 mg, given intramuscularly, did not provoke an epileptiform EEG.

Discussion

Convulsions during anesthesia are extremely dangerous and, unless promptly treated, may lead to a vegetative state.[1] Hence, rapid treatment is of primary consideration, and should be followed by an attempt to reach a diagnosis of the cause of the convulsions. This patient had a seizure following prolonged starvation and the use of methohexital sodium. Clinically, methohexital sodium is associated with involuntary

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muscle movements[2]; a literature search has failed to record any tonic–clonic seizure due to this agent. Wilder demonstrated activation of temporal lobe epileptic foci by the use of intracarotid and intravenous administration of methohexital in small doses.[3] Sleep is known to enhance epileptiform activity in psychomotor epilepsy.[4] Therefore, an EEG was performed to exclude this diagnosis.

In this patient the cause of the seizure was hypoglycemia. Over the years, anesthesiologists have commented on the occurrence of hypoglycemia with clinical signs such as lethargy, sweating, pallor, and tremulousness, which accompany the adrenergic response to a rapid decrease in blood glucose concentration.[5,6] Thomas[7] studied blood glucose levels after induction of anesthesia in two groups of children: one group was starved for as long as eight hours and another group was allowed to drink milk until four hours before anesthesia. The study, using 40 mg/dl as the level for hypoglycemia, showed that 28 per cent of children less than 47 months of age and weighing less than 15.5 kg, who had been starved, were hypoglycemic.[8,9] There was no patient with hypoglycemia in the group that had been fed until four hours prior to anesthesia. In neither group was there any sign of regurgitation or vomiting. Also found in the study was the fact that none of the children with confirmed hypoglycemia had clinical signs or symptoms of the condition. Of interest is the case report of a 5-year-old girl who underwent adenotonsillectomy and who convulsed postoperatively. At that time "no glucose was found in the blood."[10]

Once the diagnosis of a hypoglycemic seizure has been made, or even contemplated, speed is of the essence, as repeated seizures can lead to brain injury. Studies of paralyzed animals subjected to repeated seizures have demonstrated that a point is reached when the compensatory factors that increase substrate supply to a convulsing brain cannot compensate, leading to a decrease in ATP.[11] When a pediatric patient has a seizure during or after anesthesia a sample of blood for glucose determination should be obtained and an intravenous infusion of glucose started. The use of a Dextrostix is invaluable for an immediate and relatively accurate estimation. When the patient is suspected to be hypoglycemic, dextrose, 25 per cent, 2–4 ml/kg (0.5–1.0 mg/kg), is given intravenously.[12] Thereafter, one should maintain dextrose infusion at a rate of 0.5 g/kg/hr until the child can maintain an adequate blood glucose value. If, after treatment, one is still unsure of the diagnosis, a full evaluation, including measurements of blood levels of calcium, magnesium, and ketone, lumbar puncture, and EEG, should be performed.

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Anesthesiology
52:78–80, 1980

V-Lead Adapter

Donald J. Sass, Capt MC USN*

Tektronix® Models 408, 412, and 414 patient monitoring oscilloscopes were designed to record from conventional limb leads of the electrocardiogram (ECG). One can record a precordial ECG with these monitors by one of several methods that include: 1) a Tektronix 408 or 412 with modification 735D, or type 414 with option 4; 2)modified limb-lead placement[1]; 3) a V-lead adapter (013-0180-01) recently introduced by Tektronix. The modified oscilloscopes have full-lead selectors and will display precordial and limb-lead ECGs. However, one loses the option to record from limb leads when the modified limb-lead and V-lead adapter methods are used.

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PREOPERATIVE STARVATION AND BLOOD GLUCOSE CONCENTRATIONS IN CHILDREN UNDERGOING INPATIENT AND OUTPATIENT ANAESTHESIA

B. H. JENSEN, M. WERNBERG AND M. ANDERSEN

SUMMARY

Blood glucose concentrations were measured in 82 children undergoing inpatient anaesthesia and in 46 children undergoing anaesthesia as outpatients. The children were aged between 6 months and 9 yr. Outpatients were fasted from bedtime, while inpatients were randomly allocated to two groups. In group A the children were fasted from bedtime, whereas in group B the children were fed 6 h before anaesthesia. There was no difference in mean blood glucose concentration between the fasted inpatients and outpatients nor between children younger than, or older than, 4 years of age. A blood glucose concentration of less than 40 mg dl^{-1} was found in only one of the fasted children (1%). The mean blood glucose concentration was greater in group B than A, but only significantly so for children older than 4 yr. It is concluded that to minimize the risks of hypoglycaemia and inhalation of vomit on induction of anaesthesia children older than 6 months should be fasted overnight and operated on in the morning.

Since the risks of vomiting, and the inhalation of gastric contents, are inherent in the administration of general anaesthesia, established practice ordains that no patient for elective surgery be anaesthetized without a period of starvation and fluid deprivation. This period varies from 6 to 12 h or even more, in different institutions.

In studies of prolonged starvation adults were able to sustain normal glycaemic values (Cahill et al., 1966). The risk of hypoglycaemia from prolonged preoperative starvation in children was investigated by Thomas (1974), who studied the blood glucose concentrations on induction of anaesthesia in two groups of children and introduced feeding regimes in which children under 4 yr received milk or fruit syrup 4–6 h before operation.

In another study in children younger than 5 yr undergoing outpatient anaesthesia, no patient had a blood glucose concentration less than 40 mg dl^{-1}, despite at least 8 h starvation (Graham, 1979).

The purpose of the present study was to investigate the blood glucose concentrations in children undergoing inpatient and outpatient anaesthesia who were fasted and in children who received fruit syrup 6 h before inpatient anaesthesia.

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PATIENTS AND METHODS

Patients

One hundred and thirty-four otherwise healthy children, aged 6 months to 9 yr, and scheduled for elective minor surgery such as tonsillectomy, adenoidectomy and myringotomy were included in the study. The parents were informed of the purpose of the investigation and all gave their consent.

The children formed two main groups: 88 children were inpatients and 46 children were outpatients operated by a specialist outside the hospital. Each of the main groups was subdivided further into two sub-groups, group I consisting of children younger than 4 yr and group II of children greater than 4 yr.

Outpatients were all fasted from bedtime. Inpatients in both groups were randomly allocated such that some of the children were fasted from bedtime (group A) whereas others received fruit syrup and water in a dose of 7.5 ml kg^{-1} 6 h before anaesthesia (group B). The fruit syrup and water contained invertose 20 g dl^{-1}. Six children less than 4 yr refused to take the fruit syrup and were discharged from the study.

The ages, body weights and durations of starvation in the various groups are given in table I.

Anaesthesia

All children were anaesthetized in the morning. Inpatients were premedicated with nicomorphine

TABLE I. *Age, body weight, duration of starvation and blood glucose concentration before operation in 82 children undergoing inpatient and 46 children undergoing outpatient anaesthesia. Group I: Children younger than 4 yr, II: Children older than 4 yr; A: Fasting from bedtime, B: Received fruit syrup 6 h before anaesthesia. Mean values ±1 SD and range (in parentheses)*

Group	n	Age (yr)	Body weight (kg)	Duration of starvation (h)	Blood glucose concentration (mg dl^{-1})
Inpatients					
I-A	24	2.2±0.9 (0.8–3.8)	13.0±2.3 (8–17)	12.9±1.6 (7–16)	74±10 (55–102)
I-B	15	1.9±0.9 (0.5–3.8)	12.5±2.2 (9–17)		76± 9 (65–90)
II-A	22	5.9±1.7 (4–9)	21.3±4.9 (14–32)	13.6±1.5 (11–17)	72±16 (32–96)
II-B	21	5.9±1.6 (4–9)	21.8±4.9 (14–34)		82±10 (73–106)
Outpatients					
I	25	2.3±0.8 (0.7–3.5)	13.5±2.0 (9–17)	13.5±1.9 (8–16)	70± 7 (55–84)
II	21	5.7±1.7 (4–9)	20.9±4.4 (14–30)	14.5±2.0 (12–19)	70± 6 (59–81)

(Vilan) 0.2 mg kg^{-1} and atropine 0.01 mg kg^{-1}. Outpatients received no premedication. Outpatients were accompanied by a parent during the induction of anaesthesia, whereas this was not the case in inpatients. All children were anaesthetized by the inhalation of halothane in an oxygen–nitrous oxide mixture.

Measurement of blood glucose concentration

Immediately after the disappearance of the eylash reflex blood samples were withdrawn from a cubital vein. Just before venepuncture a tourniquet was placed. All venepunctures were performed by well-trained personnel. Samples were collected into fluoride bottles and analysed immediately by the o-toluidine method (Feteris, 1965). The mean of two measurements was determined. Hypoglycaemia was defined as a blood glucose concentration less than 40 mg dl^{-1}.

Statistics

The differences between groups were tested by Student's *t* test. The correlation between the period of starvation and the blood glucose concentration was estimated by Spearman's rank correlation coefficient. *P* values less than 0.05 were considered significant.

RESULTS

The mean values of the blood glucose concentrations in the different groups are given in table I. The distribution of blood glucose concentrations in all the fasted children is depicted in figure 1.

Inpatients and outpatients were comparable with respect to age and body weight whether less than, or greater than, 4 yr (groups I and II). Fasted inpatients and all outpatients were comparable with respect to their durations of starvation.

There were no differences in mean blood glucose

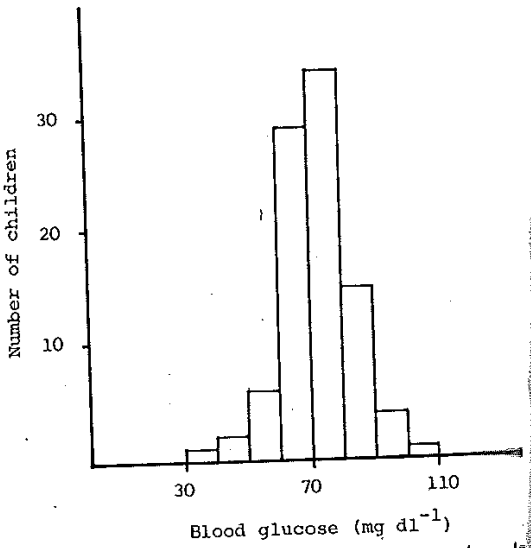

FIG. 1. Distribution of blood glucose concentrations in 92 children fasted before operation.

concentrations between the fasted inpatients (group A) and outpatients less than 4 yr ($P > 0.1$, $t = 1.34$) or greater than 4 yr ($P > 0.5$, $t = 0.58$). Likewise, there were no differences in mean blood glucose concentrations either when fasted (group A) inpatient children of groups I and II were compared ($P > 0.7$, $t = 0.34$) or when outpatients of groups I and II were compared ($P > 0.8$, $t = 0.14$).

In group I inpatients (less than 4 yr) there was no difference in mean blood glucose concentrations between groups A and B ($P > 0.3$, $t = 0.87$). However, the mean blood glucose concentration was significantly greater in group B than A in inpatients older than 4 yr (group II) ($0.02 < P < 0.03$, $t = 2.42$).

Hypoglycaemia occurred in one patient in group II-A, but not in any of the other groups. Thus, the frequency of hypoglycaemia in fasted inpatients was 2%, and in all fasted children 1%. The blood glucose concentrations in all fasted children were distributed according to a Gaussian curve (fig. 1), the distribution of the points, after probit transformation, being linear.

There was no correlation between the duration of the period of starvation and the blood glucose concentration in any of the fasted groups. For all fasted children the correlation coefficient was $r = -0.12$, $P > 0.10$.

There was no vomiting or regurgitation in either group during the induction of anaesthesia.

DISCUSSION

After the 3rd day of life hypoglycaemia is most commonly defined as a blood glucose concentration of less than 40 mg dl^{-1} (Cornblath and Schwartz, 1976; Habbick, McNeish and Stephenson, 1971).

The results of the present study are different from those obtained by Thomas (1974). In 18 children younger than 47 months he found a mean blood glucose concentration of 46.4 ± 16.5 mg dl^{-1} and 28% of the children were hypoglycaemic. The children were premedicated with trimeprazine, anaesthetized with thiopentone and the blood samples were withdrawn from the long saphenous vein, all of which differ from the present study. The effect of these differences on blood glucose concentrations is unknown, so caution must be exercised when comparing the results. The most obvious difference is that in the present study all the children were anaesthetized in the morning, while all the children in the study of Thomas (1974) were anaesthetized in the afternoon. It may be that starvation is better tolerated during the night than during the morning because of diurnal variations in metabolism. This agrees with the study of Graham (1979), who in the same hospital and using the same technique of anaesthesia as Thomas (1974) found a mean blood glucose concentration of 74 ± 3 mg dl^{-1} and no cases of hypoglycaemia following overnight fasting in 31 children less than 5 yr undergoing outpatient anaesthesia in the morning. However, contrary to the hypothesis proposed by Graham (1979), we could find no differences in mean glucose concentration between the fasted inpatients and the outpatients.

The only instance of hypoglycaemia occurred in a fasted 15-kg male child (50 months), who showed no clinical signs of hypoglycaemia before anaesthesia. The size of the child could be related to the study by Thomas (1974) since he described hypoglycaemia only in children of less than 15.5 kg body weight. According to the normal distribution of the blood glucose values in children fasting overnight, there may be a risk of hypoglycaemia during surgery. Much of this risk, however, may be avoided by adequate use of i.v dextrose during operation. In agreement with other studies (Watson, 1972; Serafimovski and Ibler, 1978; Graham, 1979) there was no correlation between the duration of the period of starvation and the blood glucose concentration.

In agreement with studies by Bevan and Burn (1973) and Thomas (1974) higher values of mean glucose concentrations were found in the groups who had been fed 6 h before anaesthesia. Thomas (1974) suggested that preoperative feeding is indicated particularly in children younger than 4 yr and weighing less than 15.5 kg, but in the present study this group showed no significant difference in mean blood glucose concentrations between the fasted and the fed children. In addition, six (29%) of the children in this group refused to receive fruit syrup in the middle of the night. Thus, preoperative feeding regimes for children older than 6 months of age, who are undergoing general anaesthesia in the morning, are of minor importance and cannot be recommended when one considers the risk of pulmonary aspiration of gastric contents. Further investigations are needed to determine the value of preoperative feeding of children less than 6 months of age.

In conclusion, to minimize the risk of hypoglycaemia and inhalation of vomit on the induction of anaesthesia, children older than 6 months should be fasted overnight and operated on in the morning.

ACKNOWLEDGEMENTS

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JEUNE PRE-OPERATOIRE ET GLYCEMIE CHEZ DES ENFANTS SOUMIS A DES ANESTHESIES, QU'ILS S'AGISSE DE PATIENTS HÔPITALISÉS OU AMBULATORES

RESUME

Nous avons mesuré la glycémie de 82 enfants hôpitalisés et de 46 enfants ambulatoires soumis à une anesthésie. L'âge des enfants était situé entre 6 mois et 9 ans. Les patients ambulatoires jeûnaient toute la nuit, et les enfants hôpitalisés étaient répartis de façon aléatoire en 2 groupes. Dans le groupe A, les enfants jeûnaient toute la nuit, tandis que dans le groupe B les enfants étaient nourris 6 h avant l'anesthésie. Il n'y a pas eu de différences entre la glycémie moyenne des enfants ambulatoires et hôpitalisés qui avaient jêuné, ni entre la glycémie moyenne des enfants âgés de moins de 4 ans ou de plus de 4 ans. On n'a retrouvé une glycémie inférieure à 0,40 mg dl^{-1} que chez un des enfants qui avaient jeûné (1%). La glycémie moyenne était plus élevée dans le groupe B que dans le groupe A mais ceci n'était significatif que pour les enfants de plus de 4 ans. Nous en concluons que pour minimiser le risque d hypoglycémie et d'inhalation de vomitus á l'induction de l'anesthśie, il faut faire jeûner toute la nuit les enfants de plus de 6 mois et les opérer le matin.

PRÄOPERATIVES HUNGERN UND BLUTGLUKOSEKONZENTRATIONEN VON KINDERN BEI AMBULANTER UND NICHTAMBULANTER NARKOSE

ZUSAMMENFASSUNG

Die Blutglukosekonzentrationen wurden bei 82 hospitalisierten Kindern und bei 46 Kindern, die eine ambulante Narkose erhielten, bestimmt. Die Kinder waren im Alter zwischen 6 Monaten und 9 Jahren. Die ambulanten Patienten mußten vom Zeitpunkt des Zubettgehens fasten, während die hospitalisierten nach Randomisierung in zwei Gruppen eingeteilt wurden. In Gruppe A mußten die Kinder vom Zubettgehen an fasten, während die kinder von Gruppe B 6 Stunden vor der Narkose Essen erhielten. Es gab keinen Unterschied zwischen den mittleren Blutglukosekonzentrationen der ambulanten und nichtambulanten Kinder die gefastet hatten, und auch nicht zwischen den Altersgruppen kleiner und größer als 4 Jahre. Eine Blutglukosekonzentration unter 40 mg dl^{-1} wurde bei nur einem der Kinder die gefastet hatten, gefunden (1%). Die mittlere Blutglukosekonzentration war in Gruppe B höher als in Gruppe A, aber signifikant nur für Kinder über 4 Jahre. Daraus kann man schließen, daß, um die Risiken der Hypoglykämie und der Aspiration von Erbrochenem bei der Narkoseeinleitung möglichst gering zu halten, Kinder über 6 Monate über Nacht fasten und am Morgen operiert werden sollten.

INANICIÓN PREOPERATORIA Y CONCENTRACIONES DE GLUCOSA EN LA SANGRE DE NIÑOS SOMETIDOS A ANESTESIA INTERNADOS EN HOSPITALES Y NO-HOSPITALIZADOS

SUMARIO

Se midío las concentraciones de glucosa en la sangre de 82 niños sometidos a anestesia e internados en el hospital así como en la de 46 niños sometidos a anestesia y no-hospitalizados. La edad de los niños variaba entre 6 meses y 9 años. Los niños no-hospitalizados estuvieron de ayunas desde la víspera al momento de acostarse, mientras que los niños hospitalizados estuvieron repartidos al azar en dos grupos. En el grupo A, los niños estuvieron de ayunas desde la víspera al momento de acostarse y los del grupo B recibieron comida 6 horas antes de la anestesia. No hubo diferencia en la concentración media de glucosa en la sangre de los niños hospitalizados y no-hospitalizados de ayunas ni tampoco entre los niños menores o mayores de 4 años. Se verificó una concentración de glucosa en la sangre de menos de 40 mg dl^{-1} en uno solo de los niños de ayunas (1%). La concentración media de glucosa en la sangre fue mayor en el grupo B que en el grupo A, pero de manera significante solamente en niños mayores de 4 años. Se llega a la conclusión que, para minimizar los riesgos de hipoglicemia o inhalación del vómito durante la inducción de la anestesia en los niños mayores de 6 meses, es necesario mantenerlos de ayunas desde la noche anterior y operarlos en la mañana.

Anaesthetic Record Set

Suggestions as to a reasonable content

PRE-OPERATIVE INFORMATION

PATIENT IDENTITY
- Name / ID No. / gender
- Date of birth

ASSESSMENT & RISK FACTORS
- Date of assessment
- Assessor, where assessed
- Weight (kg), [height (m) optional]
- Basic vital signs (BP, HR)
- Medication, incl. contraceptive drugs
- Allergies
- Addiction (alcohol, tobacco, drugs)
- Previous GAs, family history
- Potential airway problems
- Prostheses, teeth, crowns
- Investigations
- Cardiorespiratory fitness
- Other problems
- ASA ± comment

URGENCY
- Scheduled - listed on a routine list
- Urgent - resuscitated, not on a routine list
- Emergency - not fully resuscitated

PEROPERATIVE INFORMATION

CHECKS
- Nil by mouth
- Consent
- Premedication, type and effect

PLACE & TIME
- Place
- Date, start and end times

PERSONNEL
- All anaesthetists named
- Operating surgeon
- Qualified assistant present
- Duty consultant informed

OPERATION PLANNED/ PERFORMED

APPARATUS
- Check performed, anaesthetic room, theatre

VITAL SIGNS RECORDING/CHARTING
- Monitors used and vital signs (specify)

DRUGS & FLUIDS
- Dose, concentration, volume
- Cannulation
- Injection site(s), time & route
- Warmer used
- Blood loss, urine output

AIRWAY & BREATHING SYSTEM
- Route, system used
- Ventilation: type and mode
- Airway type, size, cuff, shape
- Special procedures, humidifier, filter
- Throat pack
- Difficulty

REGIONAL ANAESTHESIA
- Consent
- Block performed
- Entry site
- Needle used, aid to location
- Catheter: y/n

PATIENT POSITION & ATTACHMENTS
- Thrombosis prophylaxis
- Temperature control
- Limb positions

POSTOPERATIVE INSTRUCTIONS

Drugs, fluids and doses
Analgesic techniques
Special airway instructions, incl oxygen
Monitoring

UNTOWARD EVENTS
- Abnormalities
- Critical incidents
  - Pre-op, per-op, postoperative
  - Context, cause, effect

HAZARD FLAGS
- Warnings for future care.

Commentary

BACKGROUND

This document is produced jointly by the Royal College of Anaesthetists, The Association of Anaesthetists of Great Britain & Ireland and the Society for Computing & Technology in Anaesthesia. Work has been going on for some years to standardise the data kept about anaesthetic episodes. This is worth striving for several reasons: not only would there be a welcome agreement about what requires to be written down, but terms such as 'Start time' would be defined, and therefore reports derived from the data would be comparable.

A meeting was set up by the Society for Computing and Technology in Anaesthesia (SCATA) at the Association of Anaesthetists of Great Britain & Ireland in 1990, attended by representatives from the Royal College of Anaesthetists, and some terms used in the dataset were defined. [1] The next move was to define the content of the anaesthetic record. All concerned recognised that there is no ideal content - that what is appropriate for cardiac anaesthesia or a manipulation of a wrist are totally different, and the appropriate content must increase with the complexity of the anaesthetic. We therefore agreed to list the fields that could be included, and will later deal with the issues of what should be added. It was also fully recognised that datasets and content are continually changing; we expect that as thinking and requirements change, we will need to reissue this guidance at reasonable intervals. We also recognise that several of these definitions are contentious, and fully anticipate further serious discussion.

We have *not* attempted to design a form, but rather to show what information might be presented.

COMMENTS ON PARTICULAR FIELDS

Many items will be present 'by association' - in other words, already present in the patient's notes, and making it pointless to rewrite them. This does not diminish the need for key items of anaesthetic relevance to be copied on occasion - to emphasise that the anaesthetist was aware of them, but defining precisely which these are is not sensible.

URGENCY

This is a long debated issue, probably the most contentious in the whole set. The problem is that CEPOD uses a four division classification, *Elective*, *Scheduled*, *Urgent* and *Emergency*, and the difference between Elective and Scheduled is a purely surgical one not discernible by the anaesthetist. The CEPOD definitions were used in the dataset published in 1994.

Elective	- Operation at time to suit both patient and surgeon.
Scheduled	- An early operation but not immediately life-saving. Operation usually within 1-3 weeks.
Urgent	- Delayed operation as soon as possible after resuscitation. Operation usually within 24 hours.
Emergency	- Immediate operation, resuscitation simultaneous with surgical treatment. Operation usually within one hour.

Because of the difficulties with this classification, the 'Classes' of listed and unlisted were introduced.

Listed	- An operation published on a scheduled list
Unlisted	- Not published on a scheduled list

We are now recommending that these two classifications are amalgamated to make a more anaesthetically realistic classification that reflects daily life.

Scheduled	- listed on a routine list
Urgent	- not on a routine list, but fully resuscitated
Emergency	- not fully resuscitated

PATIENT POSITION & ATTACHMENTS

The way in which a patient was lying during anaesthesia should be recorded, including the position of the limbs and any special precautions taken against injury.

UNTOWARD EVENTS

There is a whole series of terms developing in this field - critical incidents, complications, abnormalities, negative outcomes, recovery room impact events, and more. Thinking in this field is changing sufficiently rapidly so being dogmatic about which terms to use is not sensible.

In general terms, the need is to record events so that anaesthesia may be safer in the future; to record, therefore, not only things that went wrong (complications), but also that nearly went wrong (critical incidents). We should also record 'abnormalities' such as a difficult intubation, which are not preventable, both for the patient's future safety, and for educational reasons. The severity of the incident should also be recorded.

HAZARD FLAGS

Any important abnormalities (drug sensitivities, errors of metabolism etc.) affecting the patient clearly should be flagged both on the record and in the notes.

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Further copies may be obtained from
Professional Standards Directorate
Royal College of Anaesthetists
Tel: 0171-813 1900

APRIL 1996

A revised anaesthetic record set

Professor A P Adams, Chairman, Record Working Party

In 1990 following a meeting organised by the Society for Computing and Technology in Anaesthesia (SCATA) attended by a representative of the College and the Association, a set of terms of use for anaesthetic records was defined[1]. Further meetings held with representatives from the college, AAGBI and SCATA defined the content for an anaesthetic record. Whilst no record is ideal - what is needed for cardiac surgery may well differ greatly from that needed for a simple manipulation under anaesthesia - there is a need for a starting set. The list is a start. The Working Party recognises that changes will be needed with time and intends to reissue the guide at reasonable intervals. It did not attempt to design a form but aimed to show what information might be presented. The set has been discussed and approved by the Council of the College.

Some of the items in the lists will already be present in the patient's notes and it may appear pointless to rewrite them. But several items of key information should appear on the anaesthetic chart. Four points are worthy of special note:

Urgency

There is a problem in that CEPOD uses a four-division classification - Elective, Scheduled, Urgent and Emergency. The distinction between the first two classes is purely surgical. A second classification uses: Listed and Unlisted. The Working Party proposes a more anaesthetically related classification:

- *Scheduled* - a patient listed on routine list.
- *Urgent* - a patient not on a routine list but fully resuscitated.
- *Emergency* - a patient not fully resuscitated.

Patient position and attachments

The record should note the position of the patient and the limbs together with any special precautions taken against injury.

Untoward events

There are many terms such as critical incidents, complications and negative outcomes which describe events during the perioperative period. Thinking in this field is still developing. The aim should be to make anaesthesia safer in the future by recording events where things went wrong (complications) and where they nearly did (critical incidents). Abnormalities such as difficult intubations need to be recorded.

Hazard flags

Any important abnormality such as a drug sensitivity or an error of metabolism which affects the patient should be flagged both on the anaesthetic record and in the notes.

Reference

1 Lack JA, Stuart-Taylor M, Tecklenburg A. SCATA and ESCTAIC. An anaesthetic minimum data set and report format. British Journal of Anaesthesia 1994;73:256–260.

ANAESTHETIC RECORD SET

Suggestions as to a reasonable content

The record set can be divided into groups:

PRE-OPERATIVE INFORMATION

Patient Identity

Name/Identity Number/Gender

Assessment and Risk Factors

Date of Assessment
Assessor and where assessed
Weight (kg), [height (m) optional]
Basic vital signs (BP and Heart Rate)
Medication including contraceptive drugs
Allergies
Addiction (tobacco, alcohol, drugs)
Previous general anaesthetics
Family history
Potential airway problems
Prostheses, teeth, crowns
Investigations
Cardiorespiratory fitness
Other problems
ASA status ± comment

Urgency

Scheduled – listed on a routine list
Urgent – resuscitated, not on routine list
Emergency – not fully resuscitated

PER-OPERATIVE INFORMATION

Checks

Nil by mouth
Consent to operation
Premedication, type and effect

Place and Time

Place
Date of operation
Time started and finished

Personnel

All anaesthetists named
Qualified assistant present
Operating surgeon
Duty consultant informed

Operation planned/performed

Apparatus

Checks performed, anaesthetic room and theatre

Vital Signs Recording/Charting

Monitoring used and vital signs (specify)

Drugs and Fluids

Doses, concentrations and volume
Cannulation
Injection site(s), time and route
Warmer used
Blood loss, urine output

Airway and Breathing System

Route, system used
Ventilation: type and mode
Airway type, size, cuff and shape
Special procedures, humidifier, filter
Throat pack
Difficulty

Regional anaesthesia

Consent
Block performed
Entry site
Needle used, aid to location
Catheter: yes/no

Patient Position and Attachments

Thrombosis prophylaxis
Temperature control
Limb positions

POSTOPERATIVE INSTRUCTIONS

Drugs, fluids and doses
Analgesic techniques
Special airway instructions
Oxygen therapy
Monitoring

UNTOWARD EVENTS

Abnormalities
Critical Incidents
Pre-, per- or post-operative
Context, cause and effect

HAZARD FLAGS

Warnings for future care

Hatch & Sumner 1999

index.[38,39] The inability to increase effective pulmonary blood flow and stroke volume during strenuous exercise underscores the importance of the pulmonary vascular bed in determining ventricular filling and the dependence on heart rate to increase cardiac output.

Cardiac catheterization should be considered if a patient has deteriorating symptoms or function. In particular, prior to major surgery or if significant fluid shifts are anticipated, performing a haemodynamic study under fluoroscopy immediately before surgery is often beneficial. Besides being able to assess baseline haemodynamics, a balloon-tipped catheter can be left positioned in the pulmonary artery for intraoperative and postoperative measurement of pulmonary artery pressure and mixed venous oxygen saturation. Pulmonary capillary wedge pressure can be measured to monitor the transpulmonary gradient. However, the pulmonary catheter is often difficult to wedge without direct vision because there is no pulsatile arterial pulmonary flow and the balloon may not readily float out to a lung segment. Positioning the catheter using pressure tracings alone may be difficult and direct vision using fluoroscopy is preferable. An important consideration, however, is the risk of thrombosis and obstruction to venous return after central venous line placement.

Considerations for anaesthetic management following a successful Fontan procedure are shown in Table 14.4. Ideally, the Fontan baffle, superior vena cava and branch pulmonary artery pressures should be similar in the range of 10–15 mmHg, with pulmonary venous and atrial pressure between 5 and 10 mmHg.

There are few reports in anaesthesia literature about the potential problems posed by this group of patients when presenting for non-cardiac surgery. Significant haemodynamic abnormalities may persist or develop over time, and 'correction' does not necessarily imply 'cure'. Knowledge of long-term outcome data and potential complications are important when planning anaesthesia management. The disparity between subjective or reported symptoms and objective evaluation of function often seen in these patients, highlights the value of exercise testing preoperatively as a potential means by which the response to stress during surgery and anaesthesia can be assessed.

Table 14.4 Management considerations for patients following a single-ventricle repair

	Aim	Management
Right atrium	RAp 10–15 mmHg	→ or ↑ preload
	Unobstructed venous return	Low intrathoracic pressure
Pulmonary circulation	PVR < 2 Wood units m^{-2}	Avoid increases in PVR, e.g. from acidosis, hypoinflation and hyperinflation of the lung, hypothermia and excess sympathetic stimulation
	Mean PAp < 15 mmHg	Early resumption of spontaneous respiration
	Unobstructed pulmonary vessels	
Left atrium	LAp 5–10 mmHg	Maintain sinus rhythm
	Sinus rhythm	
	Competent A-V valve	→ or ↑ rate to increase CO
	Ventricle:	
	normal diastolic function	→ or ↓ afterload
	normal systolic function	
	no outflow obstruction	→ or ↑ contractility
		Inodilators useful because of vasodilation, inotropic and lusiotropic properties

RAp, right atrial pressure; PVR, pulmonary vascular resistance; PAp, pulmonary artery pressure; LAp, left atrial pressure; A-V, atrioventricular; CO, cardiac output.

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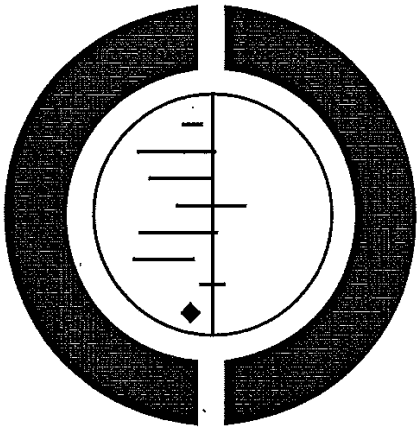
2 Murphy, J.G., Ge outcome in pati tetralogy of Fallot 1993; **329**: 593–
3 Nollert, G., Fischle survival in patient year follow-up of surgical repair. *J Cardiology* 1997;
4 Bove, E.L., Byru influence of pul function following *of Thoracic and C* 6.
5 Carvalho, J.S., Sl Exercise capacity Fallot: deleterious gitation. *British He*
6 Gatzoulis, M.A., T oelectrical interac 1995; **92**: 231–7.
7 Cullen, S., Shore, tion of right ver complete repair o **91**: 1782–9.
8 Deanfield, J.E., Mc Detection of late bances after correc *Journal* 1980; **44**:
9 Chandar, J.S., Wo arrhythmia in post *Journal of Cardiol*
10 Deanfield, J.E., M Ventricular arrhyt tetralogy of Fallot. haemodynamic st 77–81.
11 Marie, P.Y., Mar ventricular overloa tachycardia in ope *American Journal*
12 Kirklin, J.W., Blac Clinical outcomes transposition. *Circ*
13 Wernovsky, G., M influencing early a operation for trans *of Thoracic and Ca* 302.
14 Tanel, R.E., Wer Coronary artery catheterization fol for transposition of *Cardiology* 1995;
15 Weindling, S.N., Myocardial perfus

Hypotonic vs isotonic saline solutions for intravenous fluid management of acute infections (Review)

Duke T, Mathur A, Kukuruzovic RH, McGuigan M



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[Intervention Review]

Hypotonic vs isotonic saline solutions for intravenous fluid management of acute infections

Trevor Duke[1], Asish Mathur[2], Renata H Kukuruzovic[3], Michael McGuigan[4]

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Editorial group: Cochrane Injuries Group.
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ABSTRACT

Background

Hypotonic saline (such as 0.18–0.3% NaCl with dextrose) is commonly used as maintenance fluid in the management of acute infections. In recent years there have been numerous reports of hypotonic saline solutions being associated with adverse outcomes. To reduce the rates of adverse outcomes, use of isotonic saline as maintenance fluid has been proposed.

Objectives

To assess adverse events and benefits associated with infusion of hypotonic saline compared with isotonic saline solutions in the management of acute infections.

Search strategy

We searched MEDLINE, EMBASE, the Cochrane Controlled Trials Register, Current Controlled Trials and the Specialised Register of the Injuries Group.

Selection criteria

Randomised trials comparing hypotonic saline to isotonic saline in the management of acute infections.

Data collection and analysis

Three reviewers independently evaluated all potentially relevant articles, examined each study for possible inclusion and assessed the methodology quality using the Cochrane guidelines.

Main results

No trials met our inclusion criteria.

Authors' conclusions

Although there is ample evidence elsewhere that administration of large volumes of hypotonic fluids has led to severe hyponatraemia and adverse neurological outcomes in many patients with a variety of medical and surgical conditions, we found no randomised controlled trials investigating whether use of isotonic saline as maintenance fluid in those who require intravenous fluid would a be safer alternative. Careful research with adequate design and sample sizes is needed to evaluate the benefits and safety of using isotonic saline as maintenance fluid in a variety of acute clinical conditions.

PLAIN LANGUAGE SUMMARY

No evidence so far to support use of isotonic saline as a maintenance fluid instead of hypotonic saline

It is common practice to give intravenous (i.v.) fluids to patients with serious acute infections but there is no agreement as to what the sodium concentration of these fluids should be. Doctors have traditionally used intravenous fluid that contains a lower sodium concentration than is found normally in human serum; this is known as hypotonic saline. However, as patients with severe infections often have low sodium levels and adverse effects sometimes occur with the use of large amounts of hypotonic saline, it has been proposed to use intravenous fluids that have a sodium concentration similar to that of a healthy person — isotonic saline. This review has been unable to find any data from randomised trials that establish which is best.

BACKGROUND

Severe pneumonia, bronchiolitis, meningitis, malaria and septicaemia are common causes of hospital admission and mortality. Standard treatment for most such infections includes antibiotics or antimalarials, oxygen if hypoxaemia is present, fluids and nutrition. It is a common practice in hospitals to give intravenous fluids to patients with these serious acute infections. Appropriate indications include: poor tolerance of enteral fluids, risk of pulmonary aspiration (such as severe respiratory distress or poor conscious state), correction of deficits of hydration, and to maintain electrolyte balance.

There is widespread agreement among clinicians that, for resuscitation of severe hypovolaemia, boluses of isotonic saline (either 0.9% sodium chloride [0.9% NaCl or often called 'normal' saline], or albumin in saline) should be used initially. The optimal composition and volume of intravenous fluid given to seriously ill patients after initial correction of hypovolaemia, to maintain hydration and electrolyte balance during the acute illness, remains uncertain. Many patients with these serious acute infections have hyponatraemia (serum Na <130 mmol/L) at the time of presentation and many have increased antidiuretic hormone levels (Dhawan 1992; Fajardo 1989; Dixon 1988; Fryatt 1989; Kaplan 1978; Little 1975; Patwari 1995; Reynolds 1972; Rivers 1981; Shann 1985; Sharples 1992; Freidrich 1994; Miller 1967; English 1996). Many routinely receive a hypotonic intravenous solution (for example 0.18-0.3%NaCl, or occasionally even 5% dextrose with no sodium) at usual maintenance volumes (Winters 1973). When given in maintenance volumes, 0.18% NaCl (one-fifth normal saline) provides the daily sodium requirements for a well person (2–3mmol/kg/day). However, as many acutely ill patients have reduced renal water excretion, the excess free water administered may exacerbate hyponatraemia. Progressive hyponatraemia and excess free water may result in intracellular water accumulation; the most worrying effects of this are seizures, brain swelling and herniation (Halberthal 2001).

An alternative approach to fluid management aims to avoid accumulation of excess body water and development or progression of hyponatraemia. Near isotonic saline solutions (e.g. 0.9% NaCl + dextrose, or Hartmann's solution) at volumes that take account of reduced free water excretion in serious illness may achieve these aims. In serious acute infections, and in common surgical conditions, there is impaired renal free water excretion, due to increased ADH activity. ADH is also secreted in response to other non-osmotic stimuli that are common in acute illness such as nausea and vomiting. Giving isotonic saline and no electrolyte-free water will reduce the risk of exacerbating hyponatraemia (Halberthal 2001). As this approach provides greater sodium (7mmol per kilogram per day if half-traditional maintenance volumes are given as 0.9% NaCl), there may be a risk of salt and water accumulation.

The safety of this approach needs to be evaluated in a variety of conditions. Although this strategy may be optimal for a majority of serious acute infections, there may be some associated conditions where it is unwise, such as severe malnutrition, congestive heart failure or renal impairment. In these conditions, the ability to handle a salt load is impaired and the risk of cardiac failure is considerable. In many hospitals in resource-poor countries, it is not possible to measure serum electrolytes or glucose routinely, so strategies for fluid management need to be empirical and proven to be safe.

OBJECTIVES

The objective of this review is to assess whether infusion of intravenous hypotonic or isotonic saline solutions lead to different outcomes in the management of acute infections. The outcomes of interest include derangements of serum sodium, seizures, cerebral oedema, fluid overload, case fatality rates for specific conditions and neurological sequelae.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials comparing:

- hypotonic saline solutions (0.45% NaCl or less, such as 0.18% or 0.3% NaCl) with
- isotonic saline solutions (e.g. 0.9% NaCl or Hartmann's solution).

We searched for suitable trials that addressed the management of acute infections, such as meningitis, pneumonia, sepsis, malaria and bronchiolitis. Studies were included if they if they were designed to evaluate differences in the above clinical or biochemical outcomes, where at least 50% of the normal maintenance fluid volume requirements were given as intravenous fluid for 24 hours or more.

Types of participants

Patients with serious acute infections: meningitis, pneumonia, bronchiolitis, septicaemia and severe malaria. The review excluded trials in gastroenteritis, where intravenous fluid is given for replacement of existing volume deficits, and trials in premature infants, where renal salt and water handling is different to that of mature individuals.

Types of interventions

Studies where patients had received 50% or more of their daily fluid requirements as intravenous fluid, either as a hypotonic (e.g. one-fifth or one-third normal saline) or as isotonic solutions (e.g. normal saline).

Types of outcome measures

Studies measuring differences between treatment groups with regard to the following.

Acute clinical and biochemical outcomes.

These included the following.

1) Progressive hyponatraemia or hypernatraemia associated with:

- seizures
- cerebral oedema
- brain herniation
- death
- other acute neurological deterioration, while patients were receiving intravenous fluids.

2) Fluid overload, the definitions of which may include oedema of the face or body or generalised oedema, substantial weight gain or signs of pulmonary oedema.

Case fatality rates.

Long-term neurological sequelae.

Search methods for identification of studies

Electronic searches

We searched:

- Cochrane Injuries Group Specialised Register
- Cochrane Controlled Trials Register (latest issue)
- EMBASE (1980-August 2002)
- MEDLINE (1966-May 2003)
- Current Controlled Trials.

The search strategies can be found in Appendix 1.

Data collection and analysis

Results of all the searches were printed and photocopied. Three reviewers (AM, TD, RK) independently searched titles, abstracts and descriptions of all the studies identified by the electronic search. Abstracts of all potentially relevant articles were copied. Each reviewer independently examined every study, applying inclusion/ exclusion criteria. An emphasis was placed on selecting RCTs directly comparing isotonic saline with hypotonic saline, when used as a maintenance fluid in the management of acute infections. Non-randomised trials were excluded. Disagreements were resolved by discussion. While selecting the studies, we also focused on the method of randomisation, the use of allocation concealment, the use of blinding, the assessment of outcomes and exclusion of participants after randomisation.

RESULTS

Description of studies

See: Characteristics of excluded studies.

We found no randomised trials that fulfilled the inclusion criteria. Four studies (Singhi 1995; Powell 1990; Duke 2002; Neville 2003) were short-listed and examined in detail. Two studies (Singhi 1995; Duke 2002) compared two regimens of different fluid volumes, one used hypotonic saline in both the arms of the trial (Singhi 1995), and the other used 0.45% NaCl in one arm and nasogastric enteral feeds in the other (Duke 2002). One study (Singhi 1995) was terminated after enrolling 50 patients because of a trend towards a poor outcome in the patient group receiving restricted fluid volumes. However, this study was not designed to compare the effect of different fluid composition. Of the other remaining two studies, one (Powell 1990) randomised subjects to the volume of fluids, but did not specify to treating clinicians what the content of fluids should be; therefore patients received hypotonic or isotonic fluid on the basis of clinician preference. This study had a small sample size (n = 19).

On study, which is currently published in abstract only (Neville 2003), compared hypotonic saline with isotonic saline in gastroenteritis. This condition has been excluded from the list of acute infections considered for this review. Although this study does not address the conditions relevant to this review a pertinent finding was that, despite giving 0.9% NaCl with dextrose in volumes required for rehydration, hypernatraemia did not occur.

The reasons discussed above have led to the exclusion of these studies from this review.

Risk of bias in included studies

No trials included.

Effects of interventions

Not applicable.

DISCUSSION

Randomised trials directly comparing hypotonic saline with isotonic saline as maintenance fluids in the management of acute infections could not be identified in the search. The trials identified by the search strategy (Powell 1990; Singhi 1995; Duke 2002) compared volumes of fluids rather than composition. One trial that came to our attention during the review process (Neville 2003) compared hypotonic saline with isotonic saline in gastroenteritis, but this condition was excluded from the review.

There is considerable clinical observational data suggesting an association between hypotonic saline and adverse outcomes in certain conditions. In addition, there is biological plausibility that giving large volumes of hypotonic saline to patients with reduced free-water excretion will lead to hyponatraemia. However, there is currently no randomised trial evidence to determine whether isotonic saline is a better maintenance fluid than hypotonic saline.

In the absence of randomised trials of adequate size, we could not assess relative adverse events and benefits associated with infusion of hypotonic saline or isotonic saline solutions.

In the absence of randomised trials, enough data could not be generated to asses adverse events and benefits associated with infusion of hypotonic saline compared to isotonic saline solutions. This suggests a need of randomised trial evidence which will be beneficial for deciding whether isotonic saline is a better maintenance fluid than hypotonic saline in the management of acute infections or not.

AUTHORS' CONCLUSIONS

Implications for practice

The limited evidence highlighted by this review indicates that, despite strong theoretical evidence elsewhere that hypotonic intravenous fluids carry substantial risks in many seriously ill patients, the safety of using an isotonic saline as maintenance fluid has not been fully established either, at least in a direct comparison with hypotonic solutions. In maintenance fluid management there are two major issues: (1) fluid composition (in this context the amount of sodium), and (2) the fluid volume that is administered. To maintain isovolaemia most seriously ill patients, after correction of volume deficits, have reduced fluid requirements because

of high antidiuretic hormone levels. Large intravenous hypotonic fluid volumes in patients with impaired free-water excretion will carry a risk of hyponatraemia. Therefore, patients with serious infections who are requiring maintenance i.v. fluids after initial resuscitation may be least prone to major sodium imbalance if they were given isotonic saline (plus dextrose) in volumes that take account of impaired free water excretion. Currently, however, there is inadequate evidence that this strategy for fluid management will result in important differences in the incidence of adverse clinical outcomes.

Implications for research

Given the large numbers of hospitalised patients throughout the world who receive intravenous maintenance fluids, further research should be encouraged in this field. The use of isotonic saline as maintenance fluid should be evaluated in controlled trials.

It would be valuable to test the hypothesis that: isotonic saline (with 5% dextrose) at less than standard 'maintenance volumes' will result in a lower incidence of hyponatraemia, seizures and adverse neurological events than hypotonic saline solutions (0.18–0.3% saline) in acutely unwell patients with serious infections.

Ideal testing of the hypothesis would involve a large randomised controlled trial of hypotonic versus isotonic saline in the management of serious infections. However, we think it would be unethical to include some infections in such a trial. This applies particularly to encephalitis and meningitis, where there is already strong theoretical evidence and clinical experience of harm from using hypotonic intravenous fluid, especially at or near maintenance volumes, and where there is a higher risk of cerebral oedema and adverse outcomes if hyponatraemia occurs. An alternative approach in hospitals where hypotonic fluids are the routine standard of care would be to change the policy such that isotonic saline becomes the standard background intravenous fluid, and to carefully audit the change. Although not as robust as an RCT, this would allow for a detailed before and after analysis. Outcomes could include differences in the proportions of patients who suffer neurological events associated with progressive hyponatraemia. Evaluation of safety could include differences in the frequency of severe hypernatraemia, the occurrence of neurological complications associated with rapidly rising serum sodium, or fluid retention.

ACKNOWLEDGEMENTS

We are grateful to the Royal Children's Hospital, Melbourne librarians Cathy Gatt and Poh Chua for their valuable support and guidance in designing and conducting the electronic search for this review.

We wish to thank Professor Ian Roberts (Coordinating Editor), Paul Chinnock (Managing Editor) and Katharine Ker (Review Group Coordinator) of Cochrane Injuries Group for their assistance and support during the preparation of this review.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of excluded studies *[ordered by study ID]*

Duke 2002	The study did not compare the content of fluids given to the patients i.e. hypotonic or isotonic. Patients in both the groups received a hypotonic solution either as nasogastric feed or intravenous infusion.
Neville 2003	Abstract only. The trial was comparing fluids in the management of gastroenteritis. The fluids were given in this study as re-hydration fluids and not as maintenance volumes.
Powell 1990	The patients were randomized to the volumes of fluids and not the content i.e. hypotonic or isotonic. The methodological quality of the trial was poor in that it did not specify which group of patients received hypotonic or isotonic saline and therefore the results could be subject to bias.
Singhi 1995	Randomization was done on the basis of fluid volumes and not the content. Patients in both the groups received a hypotonic saline.

DATA AND ANALYSES

This review has no analyses.

WHAT'S NEW

Last assessed as up-to-date: 13 May 2003.

11 July 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 2, 2003

Review first published: Issue 2, 2004

CONTRIBUTIONS OF AUTHORS

Asish Mathur and Trevor Duke conceived the idea, designed and coordinated the review along with screening search results, retrieval of papers, screening retrieved papers against inclusion criteria, appraising quality of papers, methodological perspective, data entry into RevMan, analysis of data, clinical perspective and writing of the Review.

Renata Kukuruzovic contributed in screening search results, retrieval of papers, screening retrieved papers against inclusion criteria, appraising quality of papers, methodological perspective and writing of the Review.

Mike South: Clinical perspective

DECLARATIONS OF INTEREST

None known.

INDEX TERMS

Medical Subject Headings (MeSH)

Acute Disease; Fluid Therapy [*methods]; Infection [*therapy]; Isotonic Solutions [therapeutic use]; Sodium Chloride [*therapeutic use]

ORIGINAL ARTICLE

Isotonic is better than hypotonic saline for intravenous rehydration of children with gastroenteritis: a prospective randomised study

K A Neville, C F Verge, A R Rosenberg, M W O'Meara, J L Walker

Arch Dis Child 2006;91:226–232. doi: 10.1136/adc.2005.084103

See end of article for authors' affiliations

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Accepted 29 November 2005
Published Online First 13 December 2005

Aims: To determine whether the risk of hyponatraemia in children with gastroenteritis receiving intravenous (IV) fluids is decreased by the use of 0.9% saline.
Methods: A prospective randomised study was carried out in a tertiary paediatric hospital. A total of 102 children with gastroenteritis were randomised to receive either 0.9% saline + 2.5% dextrose (NS) or 0.45% saline + 2.5% dextrose (N/2) at a rate determined by their treating physician according to hospital guidelines and clinical judgement. Plasma electrolytes, osmolality, and plasma glucose were measured before (T_0) and 4 hours after (T_4) starting IV fluids, and subsequently if clinically indicated. Electrolytes and osmolality were measured in urine samples. Results were analysed according to whether children were hyponatraemic (plasma sodium <135 mmol/l) or normonatraemic at T_0.
Results: At T_0, mean (SD) plasma sodium was 135 (3.3) mmol/l (range 124–142), with 37/102 (36%) hyponatraemic. At T_4, mean plasma sodium in children receiving N/2 remained unchanged in those initially hyponatraemic (n = 16), but fell 2.3 (2.2) mmol/l in the normonatraemic group. In contrast, among children receiving NS, mean plasma sodium was 2.4 (2.0) mmol/l higher in those hyponatraemic at baseline (n = 21) and unchanged in the initially normonatraemic children. In 16 children who were still receiving IV fluids at 24 hours, 3/8 receiving N/2 were hyponatraemic compared with 0/8 receiving NS. No child became hypernatraemic.
Conclusions: In gastroenteritis treated with intravenous fluids, normal saline is preferable to hypotonic saline because it protects against hyponatraemia without causing hypernatraemia.

Recent publications[1–3] have highlighted the potential for life threatening hyponatraemia associated with the use of intravenous hypotonic saline in hospitalised children, including children with gastroenteritis.[2 4] Although most guidelines recommend low osmolarity oral rehydration solutions for rehydration of children with mild to moderate dehydration secondary to non-cholera gastroenteritis,[5–7] intravenous fluids are frequently used when oral rehydration is not tolerated, particularly in developed countries.[8–10] There is no consensus however on the most appropriate electrolyte composition of intravenous (IV) fluids, with recommendations ranging from 0.45% to 0.9% saline solutions.[5–7 11] Previously, we have documented antidiuretic hormone (ADH) activity inappropriate for the plasma sodium and osmolality in children receiving intravenous fluids for mild to moderate dehydration associated with gastroenteritis.[12] While this could cause dilutional hyponatraemia irrespective of the saline content of the fluid, the use of a fluid with a higher tonicity presenting less electrolyte free water should reduce this risk.[1 13]

To explore this, we studied the changes in blood and urine biochemistry in children with a presumptive diagnosis of gastroenteritis in whom a decision to treat with IV fluids had been made by their treating physician. Apart from randomisation to either normal or half normal saline, other aspects of management, including fluid rate, were determined by the treating physician based on hospital guidelines and clinical judgement. As we found previously that the biochemical response to IV fluids differed according to the plasma sodium at presentation,[12] we analysed the results according to whether children were hyponatraemic or normonatraemic at presentation.

METHODS

The study was conducted at Sydney Children's Hospital between the months of August and October 2002, corresponding to the annual peak incidence of rotavirus infection.[14] Children aged between 6 months and 14 years with a presumptive diagnosis of gastroenteritis were eligible for enrolment in the study only after a decision to treat with intravenous (IV) fluids had been made by their treating physician, independent of the study (fig 1). The reasons recorded for this decision were the combination of dehydration and either continued vomiting or inadequate intake of oral fluids in the emergency department. Children were excluded from the study if they had a known abnormality of ADH secretion, nephrogenic diabetes insipidus, pituitary or hypothalamic disease, renal disease, acute or chronic lung disease, or were receiving drugs known to stimulate ADH secretion. The study protocol was approved by the South Eastern Area Research Ethics Committee and informed consent was obtained from a parent/guardian of all children.

At enrolment, children were prospectively randomised to receive either 0.45% saline + 2.5% dextrose (N/2) or 0.9% saline + 2.5% dextrose (NS) by sequential selection of an opaque sealed envelope containing the fluid choice. The treating physician was told which fluid had been selected. The rate of infusion was not randomised, but was determined by the treating physician according to one of two clinical protocols in use in the emergency department: the "rapid replacement protocol" (RRP; 10 ml/kg/h for 4 hours), or the "slow replacement protocol" (SRP; maintenance fluids[15] +

Abbreviations: ADH, antidiuretic hormone; IV, intravenous; RRP, rapid replacement protocol; SRP, slow replacement protocol

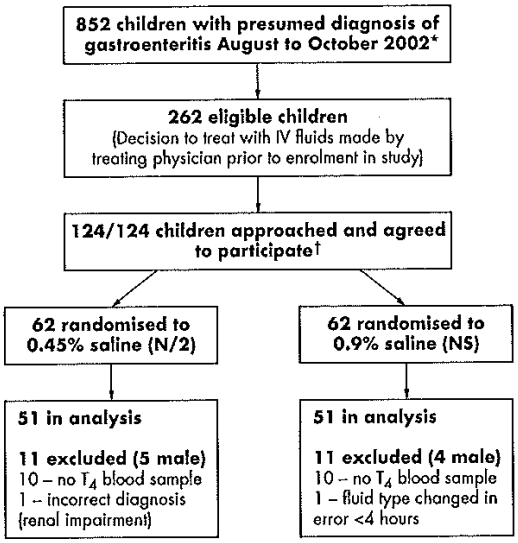

Figure 1 Flow diagram of patient selection. *Corresponding to the annual peak incidence of rotavirus infection. †A registered nurse was employed 40 hours per week (including weekends and after hours) to facilitate the correct administration of the study protocol in a busy emergency department. Enrolment was carried out only during her shifts.

estimated dehydration as a percentage of body weight replaced over 24 hours). Blood samples were collected before (T_0) and 4 hours after (T_4) the start of IV fluids, with the T_4 measurement corresponding to completion of the RRP. The study protocol permitted the treating physician to change the fluid type after the first 4 hours of infusion. However this was done in two patients only: one child was changed from NS to N/2 at 5 hours because the plasma sodium concentration had increased from 130 to 135 mmol/l; and one was changed from N/2 to NS at 10 hours because the plasma sodium concentration remained below 135 mmol/l.

Details of the illness prior to presentation were recorded. The admission weight, length (in children under 2 years), or height and body mass index (BMI; weight/height^2) were expressed as standard deviation scores (SDS)[16 17] to allow comparison across ages. The degree of dehydration at presentation was estimated using standard clinical measures.[18] Stools for culture and rotavirus antigen testing were obtained in 35/102 children, 30 of which were positive for rotavirus antigen. There were no differences in the historical, clinical, or biochemical characteristics at presentation or the fluid rate received, comparing the 51 children who received N/2 with the 51 who received NS (table 1) as would be expected from the randomisation.

The blood samples were analysed for the concentrations of sodium, potassium, bicarbonate, urea, and creatinine using ion selective electrodes, glucose using an oxygen rate method, and osmolality using freezing point depression. Urine sample collection via urine bag in incontinent children and clean catch specimens in toilet trained children was attempted for the determination of sodium and potassium concentrations, tonicity (urinary sodium plus potassium concentration), and osmolality. In addition, ketonuria was assessed by Ketodiastix (Bayer Clinitest 50, Bridgend, South Wales, UK) in the first urine specimen passed; the results were recorded as either absent, trace, small, moderate, or large. A sample of the first urine passed was collected in 76/102 children, in only 43 of whom was it passed between −1 and +2 hours of T_0, consistent with this being a dehydrated population. In 36/43 children a subsequent urine specimen (U_{2nd}) was obtained between 3 and 12 hours (median 4.8 hours) after T_0, allowing analysis of the change in electrolytes and osmolality.

The short term response of plasma and urinary electrolytes and osmolality to treatment was analysed according to whether the children were hyponatraemic (plasma sodium <135 mmol/l) or normonatraemic at T_0. A change in plasma sodium of ⩾2 mmol/l was considered to be biochemically significant as this exceeds the coefficient of variation (CV) of the assay for the laboratory reference range of 135–145 mmol/l (CV 1.3–1.5%).

To gauge the prevalence of hypo- or hypernatraemia during prolonged fluid administration, plasma and urinary data in 42/102 children (22 N/2) whose IV fluids were continued for >4 hours were analysed in each child. Variable data on each child were available (between 8 and 31 hours after T_0) depending on the duration of IV infusion.

Statistical analysis

All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, version 11.0 for Windows). Results were expressed as either mean (SD) or median (range) unless otherwise indicated. Means between groups were compared by independent t tests and paired variables by paired sample t tests. Medians were compared by the Mann-Whitney U test and changes over time were compared by the Wilcoxon signed rank test. Categorical data were analysed using cross tabulation and the χ^2 test or Fisher's exact test if two cells had expected counts less than 5. Statistical significance was defined as a p value less than 0.05.

RESULTS

Baseline clinical and biochemical characteristics

The mean (SD) plasma sodium concentration at T_0 in the 102 children was 135 (3.3) mmol/l (range 124–142). Thirty seven of the children (36%) were hyponatraemic at T_0, four of whom had a plasma sodium concentration less than 130 mmol/l. The median length of illness prior to presentation was longer in the hyponatraemic children (2 days, range <24 hours to 5 days) compared with the normonatraemic children (1 day, range <24 hours to 7 days; $p < 0.01$) and the mean BMI SDS was lower (−0.7 (1.2) v −0.1 (1.1); $p < 0.01$). Comparing the children who were hyponatraemic versus those who were normonatraemic at T_0, there were no differences in age (mean 2.8 (1.3) years v 2.9 (2.0) years; $p = 0.72$), sex (51% v 46% male; $p = 0.61$), percent dehydration (median 5% (range 3–7) v 5% (range 3–7); $p = 0.27$), rotavirus positivity (12/13 v 18/22 tested; $p = 0.74$), or the type (43% v 53% N/2; $p = 0.30$) or rate (78% v 75% RRP; $p = 0.73$) of intravenous fluids subsequently received.

The first urine was passed a median of 2.3 hours (range −1.0 to 13.5) after starting intravenous fluids. In the 76/102 in whom this was collected, the median urinary sodium concentration was higher in samples containing "moderate" or "large" ketones (57/76; 58 mmol/l, range <10–209) compared with those that were negative for ketones or had only trace or small amounts (19/76; 20 mmol/l, range <10–109; $p < 0.01$).

In the 43 children for whom a urine sample was passed and obtained within 2 hours of T_0, the median urinary osmolality was 971 mOsm/kg (range 315–1290 mOsm/kg), median urinary sodium concentration was 58 mmol/l (range <10–209 mmol/l), and median urinary potassium 71 mmol/l (range 13–232). The median urinary tonicity (urinary

Table 1 Baseline clinical and biochemical characteristics of the children randomly assigned to receive either 0.45% saline (N/2) or 0.9% saline (NS)

	N/2 n=51	NS n=51
M/F	30/21	23/28
Age, years*	3.1 (2.0)	2.7 (1.5)
% dehydrated†	5 (3–7)	5 (3–7)
Height SDS*‡	0.4 (1.1)	0.5 (1.3)
Weight SDS*‡	0.0 (1.1)	0.1 (0.9)
BMI SDS*‡	−0.4 (1.2)	−0.3 (1.2)
Duration of illness prior†	1 day (<24h–7d)	2 days (<24h–5d)
Presenting symptoms, n (%)		
Vomiting illness only	18 (35%)	11 (22%)
Diarrhoea only	1 (2%)	1 (2%)
Vomiting and diarrhoea	32 (63%)	39 (77%)
Fluid rate initiated		
RRP	40/51	38/51
SRP	11/51	13/51
Plasma biochemistry*		
Sodium, mmol/l	136 (2.8)	135 (3.6)
Potassium, mmol/l	4.0 (0.5)	4.0 (0.5)
Bicarbonate, mmol/l	17.9 (2.9)	17.8 (3.0)
Urea, mmol/l	5.1 (1.9)	5.6 (1.9)
Creatinine, µmol/l	46.6 (12.2)	45.9 (10.4)
Glucose, mmol/l§	4.3 (1.1)	4.4 (1.1)
Osmolality, mOsm/kg	281 (7)	281 (8)
Hyponatraemia (plasma Na <135 mmol/l) at T_0, n (%)	16/51 (31%)	23/51 (41%)
Urine biochemistry†¶	n=23	n=20
Sodium, mmol/l	58 (<10–204)	63 (<10–209)
Potassium, mmol/l	71 (13–171)	70 (19–232)
Tonicity (sodium + potassium), mmol/l	161 (19–285)	153 (26–300)
Osmolality, mOsm/kg	973 (315–1290)	1004 (574–1200)

SDS, standard deviation score.
Results are expressed as either *mean (SD) or †median (range). As expected from randomisation, there were no significant differences between the groups. The rate of IV fluids received conformed to either the rapid replacement protocol (RRP) or slow replacement protocol (SRP) at the discretion of the treating physician.
‡The admission weight, length (in children under 2 years), or height and body mass index (BMI; weight/height^2) were expressed as standard deviation scores (SDS) to allow comparison across ages.
§Four children aged between 0.9 and 3.7 years had blood glucose concentrations at T_0 of between 2.0 and 2.6 mmol/l. The hypoglycaemia responded to the 2.5% dextrose content of each study fluid and subsequent investigations excluded a second pathology.
¶Analysis of urine samples collected in 43 of 49 children who passed urine between −1 and +2 hours of starting IV fluids.

concentrations of sodium + potassium) was 161 mmol/l (range 19–300), approximately that of normal saline (154 mmol/l). The urinary sodium, tonicity, and osmolality were similar in the NS (20/43) and N/2 (23/43) groups (table 1) and were independent of whether children were hyponatraemic (16/43) or normonatraemic (27/43) at baseline (hyponatraemic versus normonatraemic children: median urinary sodium 52 (range <10 to 204) *v* 70 (range <10 to 209), p = 0.39; median urinary tonicity 131 mmol/l (range 19 to 285) *v* 163 mmol/l (range 22 to 300), p = 0.1; median urinary osmolality 935 (range 315 to 1290) *v* 1036 (range 356 to 1239), p = 0.35). The median urinary potassium however was lower in the hyponatraemic children (68 (range 13–91) *v* 89 (range 16–232), p = 0.03).

Effect of IV fluid infusion rate on change in plasma sodium

The infusion rate (RRP versus SRP) was not a determinant of the change in plasma sodium in either treatment arm.

In the NS group, those treated with the RRP (38/51) had a median change in sodium of +1 mmol/l (range −7 to 6) versus SRP +2 mmol/l (range −1 to 8) (p = 0.08). In children receiving N/2 the median change in plasma sodium in those who received RRP (40/51) was −1 mmol/l (range −6 to +2) versus −1 (range −5 to +3) in those treated according to the SRP (p = 0.92, Mann-Whitney U test).

Effect of IV fluid type on plasma sodium at T_4

The plasma sodium response to N/2 versus NS differed depending on whether the children were hyponatraemic or normonatraemic initially.

After 4 hours rehydration with N/2, the mean plasma sodium had not changed in the hyponatraemic children (p = 0.32) but had decreased significantly in the initially normonatraemic group (p < 0.001; table 2, fig 2). In the normonatraemic group, plasma sodium decreased by ≥2 mmol/l in 51% (18/35) compared with 13% (2/16) in the hyponatraemic group (p < 0.001; table 2). In 20% of the initially normonatraemic children (7/35), the fall was ≥5 mmol/l. The maximum decrease was 6 mmol/l in two children treated with N/2 by RRP. The maximum increase in plasma sodium over 4 hours was 3 mmol/l in a child treated with N/2 by SRP.

In contrast, after 4 hours rehydration with NS, there was a mean increase in plasma sodium of 2.4 (1.5) mmol/l in children who were initially hyponatraemic (p < 0.001) compared with no significant change in the normonatraemic group (p = 0.08; table 2, fig 2). Thirteen per cent (4/30) of the normonatraemic group and none of the hyponatraemic group experienced a decrease in plasma sodium of ≥2 mmol/l (table 2). The maximum decrease in plasma sodium concentration was 7 mmol/l (140 to 133 mmol/l) in a normonatraemic child, in whom fluids were discontinued

Table 2 Mean (SD) plasma sodium and osmolality at baseline (T_0) and after 4 hours of intravenous rehydration (T_4) in the initially hyponatraemic (plasma sodium <135 mmol/l) versus normonatraemic (plasma sodium 135–145 mmol/l) children who received either 0.45% saline + 2.5% dextrose (N/2) or 0.9% saline + 2.5% dextrose (NS)

	N/2 (n=51)			NS (n=51)		
	Hyponatraemic (n=16)	Normonatraemic (n=35)	p value	Hyponatraemic (n=21)	Normonatraemic (n=30)	p value
T_0 sodium (mmol/l)	132 (1.5)	137 (1.7)		132 (2.4)	137 (2.2)	
T_4 sodium (mmol/l)	133 (1.8)	135 (1.8)*	<0.001	134 (2.1)*	138 (2.9)	<0.001
Change in sodium (mmol/l)	+0.4 (1.7)	−2.3 (2.2)	<0.001	+2.4 (2.0)†	+0.8 (2.4)‡	0.02
Sodium decreased ≥ 2 mmol/l from 0–4 hours	13% (2/16)	51% (18/35)	<0.01	0% (0/21)	13% (4/30)	0.13
T_0 osmolality (mOsm/kg)	277 (6.3)	283 (7.2)	0.005	277 (6.9)	284 (6.9)	0.001
T_4 osmolality (mOsm/kg)	276 (4.4)	278*(5.0)	0.21	279 (4.3)	283 (6.7)	0.01

*p<0.001, T_4 versus T_0.
†p=0.003, hyponatraemic children NS versus N/2.
‡p<0.001, normonatraemic children NS versus N/2.

at completion of the RRP; it was associated with an inappropriately high urinary sodium concentration in concentrated urine at 6 hours (urinary sodium 76 mmol/l, potassium 94 mmol/l, tonicity 170 mmol/l, osmolality 885 mOsm/kg). The maximum increase in plasma sodium over 4 hours was 8 mmol/l, from 124 to 132 mmol/l in a child treated with NS by SRP. Plasma osmolality changes in all groups were consistent with changes in plasma sodium (Table 2).

Response of urinary sodium, tonicity, and osmolality to IV fluids

To assess the response of urinary electrolytes and osmolality to IV fluids, only the 36 children with a baseline (U_{base}) and subsequent (U_{2nd}) urine sample were analysed (table 3). Apart from being slightly older than the rest of the study group (median 3.8 years (range 1.1–11.9) *v* 2.0 years (range 0.8–7.5); $p < 0.001$), the 36 children's clinical and biochemical data (T_0 and T_4) were comparable with the group as a whole. Nineteen received NS and 17/36 received N/2. Eight children in each group were hyponatraemic at T_0.

Irrespective of the fluid received or the plasma sodium at T_0, urinary potassium concentration decreased (table 3), which would be consistent with a decrease in aldosterone secretion following volume expansion. In contrast, the urinary concentration of sodium in the second sample varied according to the initial plasma sodium concentration and the fluid received. The urinary concentration of sodium decreased in the hyponatraemic children treated with NS and tended to do so in those receiving N/2 (table 3), whereas it increased in the normonatraemic children receiving NS and did not change in those receiving N/2 (table 3).

In keeping with the changes in concentration of sodium and potassium, the median urinary tonicity of the second urine sample had decreased significantly in the hyponatraemic children (table 3) to less than that of half normal saline. In the normonatraemic children, the median urinary tonicity decreased, but remained above that of half normal saline in the N/2 group and remained approximately that of normal saline in the NS group.

Median urine osmolality decreased in both treatment groups irrespective of the initial plasma sodium (table 3).

Biochemical changes during more prolonged fluid administration

Forty two children (22 N/2 and 20 NS) received IV fluids for more than 4 hours. These comprised all 24/102 children who

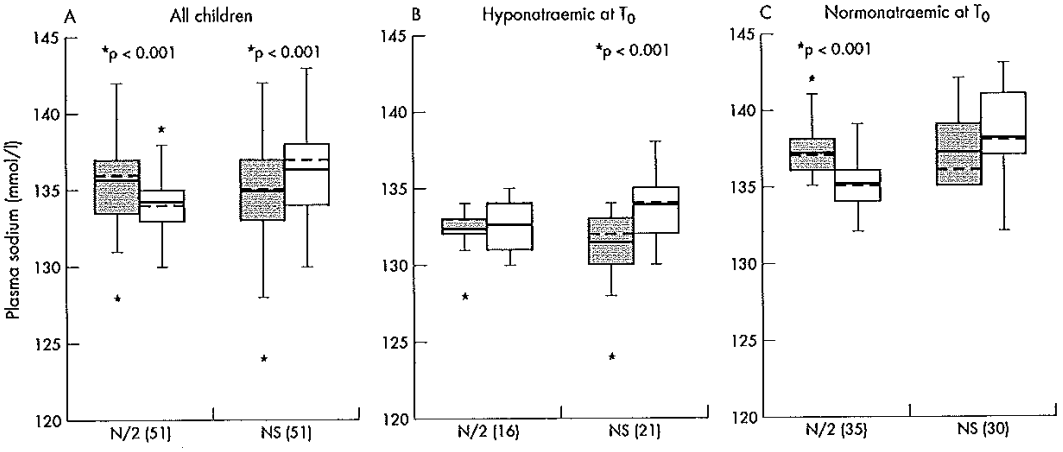

Figure 2 Box plots showing the plasma sodium concentration at baseline (T_0; shaded) and after 4 hours (T_4; white) infusion of either N/2 or NS in (A) all children and those who were either (B) hyponatraemic or (C) normonatraemic prior to starting IV fluids. Box plots show the mean (solid horizontal line), median (dashed horizontal line), interquartile range (box limits), and minimum and maximum (whiskers), except that extreme outliers (greater than 1.5 box lengths from the edge of the box) are shown as individual data points. In the N/2 group, mean plasma sodium concentration did not change in the initially hyponatraemic children and decreased in the initially normonatraemic children. In the NS group however, mean plasma sodium increased in the hyponatraemic children and did not change in the normonatraemic children. No child became hypernatraemic.
*Paired *t* test T_4 *v* T_0.

Table 3 Response of urinary sodium, potassium, tonicity (Na + K), and osmolality to either N/2 or NS, according to whether the children were hyponatraemic or normonatraemic at T_0 in the 36 children in whom a baseline urine sample (U_{base}) was collected within 2 hours of T_0, and a second sample (U_{2nd}) was collected a median of 4.8 hours (range 3–12) after T_0

	Hyponatraemic at T_0						Normonatraemic at T_0					
	N/2 (n = 8)			NS (n = 8)			N/2 (n = 9)			NS (n = 11)		
	U_{base}	U_{2nd}	p value	U_{base}	U_{2nd}	p value	U_{base}	U_{2nd}	p value	U_{base}	U_{2nd}	p value
Na (mmol/l)	72 (<10–204)	23 (<10–82)	0.09	38 (<10–109)	16 (<10–75)	0.04	80 (16–124)	59 (10–123)	0.44	79 (17–209)	125 (19–294)	0.01
K (mmol/l)	70 (12–91)	23 (4–38)	0.02	58 (19–88)	24 (6–65)	0.02	105 (57–171)	47 (10–74)	0.008	107 (42–232)	39 (3–94)	0.003
Tonicity (mmol/l)	151 (19–285)	45 (11–109)	0.02	106 (26–175)	40 (14–140)	0.02	178 (146–213)	104 (67–170)	0.008	183 (59–300)	165 (46–322)	0.63
Osmolality (mOsm/kg)	976 (332–1290)	506 (110–944)	0.02	935 (574–1072)	768 (339–1059)	0.02	1036 (856–1239)	668 (284–1139)	0.008	1076 (707–1200)	881 (317–1177)	0.006

Results are expressed as median (range).
The p values refer to the comparison by Kruskall Wallis test of U_{2nd} with U_{base}.

were treated according to the SRP (table 1) plus 18/78 (11 N/2, 7 NS) who completed the RRP but continued IV fluids according to the SRP because of continued vomiting or poor oral fluid intake. Plasma biochemistry at T_4 was similar to that of the group as a whole (data not shown). Plasma sodium concentrations were available at 24 hours in 16 children (8 N/2) who continued to receive at least half of their maintenance requirement of fluid[15] intravenously, at which time no child receiving NS had a plasma sodium <135 mmol/l (range 135–142 mmol/l) compared with 3/8 of the N/2 group (range 131–140 mmol/l). The maximum increase in plasma sodium over 24 hours was 12 mmol/l to 136 mmol/l in a child receiving NS.

To gauge the potential for clinically significant dilutional hyponatraemia among the 42 children who received prolonged IV fluids, each individual's longitudinal biochemical data were studied. Five of the 22 treated with N/2 but none treated with NS (N/2 *v* NS: p = 0.03, Fisher's exact test) had persistent significant hyponatraemia (sodium ⩽ 131 mmol/l) or falls in plasma sodium ⩾4 mmol/l to below 135 mmol/l associated with an inappropriately high urinary sodium content (range 30–140 mmol/l) and urine osmolality higher than plasma osmolality (range 462–1058 mOsm/kg), suggesting that they were at risk of dilutional hyponatraemia. The plasma and urinary abnormalities were documented to persist for a median of 19 hours (range 8–27).

As no child who received prolonged NS developed this problem, we analysed data from the 22 children who received N/2 for more than 4 hours to identify potential clinical or biochemical predictors that could allow early detection of those at risk. Comparing the five children who developed significant dilutional hyponatraemia with the remaining 17/22, no clinical or biochemical parameters emerged that would allow early identification of those at risk, except for continuation of IV fluids beyond 4 hours after completion of the RRP (completion of RRP: 5/5 affected *v* 6/17 unaffected; p = 0.04). Apart from a slightly higher median urea (6.8 mmol/l (range 5.3–9.1) *v* 5.1 mmol/l (range 1.2–8.7); p = 0.02) suggestive of more severe dehydration, there were no differences in their median age (p = 0.09), BMI SDS (p = 0.24), estimated degree of dehydration (p = 0.54), length of illness prior to presentation (p = 0.49), baseline plasma sodium (p = 0.82), bicarbonate (p = 0.09), or creatinine (p = 0.14). Three of the five children had stool cultures performed, all of whom were positive for rotavirus.

DISCUSSION

Recently, the basis for the use of intravenous hypotonic saline solutions in sick children has been questioned and it has been suggested that the use of isotonic saline solutions might decrease the frequency of iatrogenic hyponatraemia.[1 2 13] In this prospective, randomised study we have shown that when children with gastroenteritis are treated with intravenous fluids, hyponatraemia is less likely to develop or persist if an isotonic rather than hypotonic saline solution is used.

The baseline clinical and biochemical characteristics of the 102 children in our current report were similar to those in our previous study.[12] Hyponatraemia was common at presentation (36%). This has been attributed to the sodium content of diarrhoeal losses[19 20] and low salt intake;[19] but the inappropriately high urinary sodium content we again documented at presentation may also contribute. The relationship we observed between the sodium concentration in the first urine sample passed and the degree of ketonuria suggests that the excretion of ketones as sodium salts may have contributed to the relatively high urinary sodium concentrations, consistent with reported association between natriuresis and starvation.[19 21]

What is already known on this topic

- Hyponatraemia in hospitalised children, including those with gastroenteritis, is common and can be associated with cerebral oedema and death
- Hypotonic saline solutions are frequently used in children and have been suggested to contribute to the development of hyponatraemia

What this study adds

- Biochemical evidence shows that in children with gastroenteritis, hypotonic saline solutions exacerbate the tendency to develop dilutional hyponatraemia while isotonic saline solutions are protective
- Urinary biochemistry suggests that isotonic solutions are safe because hyponatraemic children retain sodium and normonatraemic children excrete it appropriately

Non-osmotic ADH activity is thought to underlie the development of hospital acquired dilutional hyponatraemia by preventing the excretion of electrolyte free water during fluid administration.[3 22] Gerigk and colleagues[23] documented raised ADH levels independent of osmolality in children with a variety of common acute childhood illnesses and we have reported that osmotically inappropriate ADH activity is common and persistent in children with gastroenteritis.[12] Consistent with this, the biochemical response to N/2 was almost identical in this and our previous study[12] in which all of the children received N/2. In both studies, the mean plasma sodium concentrations of children who were initially normonatraemic decreased, and those of children who were hyponatraemic did not improve in response to N/2. Half the normonatraemic children and 13% of the hyponatraemic children treated with N/2 experienced a decrease in plasma sodium ≥2 mmol/l, and after 24 hours, 3 of 8 children largely dependent on IV fluids were hyponatraemic. In contrast, the use of isotonic saline over 4 hours resulted in maintenance of plasma sodium in those initially normonatraemic and an increase in those initially hyponatraemic. None developed hypernatraemia. After 24 hours, all 8/51 children still receiving normal saline were normonatraemic. Five of the 22 (23%) who received prolonged half-normal saline displayed biochemistry suggestive of dilutional hyponatraemia, compared with none of the 20 treated with normal saline. These findings suggest that in children with gastroenteritis, the use of hypotonic fluids exacerbates the tendency to develop hyponatraemia whereas the use of isotonic saline is protective.

The urinary biochemistry may provide some basis for understanding the decreased risk of hyponatraemia in children given isotonic saline and is reassuring with respect to the risk of hypernatraemia. As seen in our previous study,[12] despite mild to moderate dehydration and irrespective of the plasma sodium concentration, the median urinary sodium concentration at presentation approximated that of half-normal saline and the urinary tonicity approximated that of normal saline. Urinary tonicity is a better reflection of free water clearance than urinary osmolality[24] because an important component of osmolality is urea, which readily crosses cell membranes and therefore does not influence water movement. Administration of a fluid of lower tonicity than that of the urine being passed is predicted to result in a decrease in plasma sodium concentration because of the retention of free water implicit in the excretion of urine with a higher tonicity. After several hours of IV fluids, the urinary potassium decreased in all children in our study and the median urinary sodium concentrations of the hyponatraemic children in both treatment groups had decreased to levels consistent with maximal renal conservation of sodium (approximately 20 mmol/l;[25 26] table 3); thus the urinary tonicity of the hyponatraemic children had decreased to less than the tonicity of N/2. As a result, the plasma sodium concentrations of the hyponatraemic children receiving hypotonic saline were maintained (but not improved) over 4 hours, whereas plasma sodium increased in the hyponatraemic children who received NS, a fluid roughly isotonic with respect to their initial urinary tonicity. The normonatraemic children on the other hand, did not conserve sodium. Although urinary potassium excretion decreased in these children, the median urinary concentration of sodium was unchanged in the N/2 group and increased in the NS group. The normonatraemic children treated with N/2 therefore continued to excrete urine that was hypertonic relative to the infused fluid. This would explain the accompanying decrease in plasma sodium concentration. Those given NS continued to excrete urine isotonic with respect to the infused fluid and maintained their plasma sodium concentration unchanged.

The basis of the greater renal avidity for sodium in the hyponatraemic compared with the normonatraemic children is unclear. A similar phenomenon has been described in rats infused simultaneously with normal saline and ADH, in whom those fed a salt poor diet prior to the infusion were better able to retain sodium and maintain their plasma sodium than those whose dietary content of salt had been normal.[27] The median duration of illness was longer in the hyponatraemic children and therefore, in addition to more prolonged sodium losses in diarrhoeal stools[19] and urine,[12] their dietary intake of sodium is likely to have been lower than for those children who were normonatraemic at presentation. Relatively chronic sodium depletion therefore may have promoted the development of renal adaptive responses, resulting in more rapid reversal of the natriuresis evident at presentation. Differential suppression of aldosterone activity in the normonatraemic versus hyponatraemic children during fluid therapy might have contributed if the hyponatraemic children were more dehydrated at baseline; however there were no clinical or biochemical data to support this. Furthermore, the similar decrease in urinary potassium in the hyponatraemic and normonatraemic children and significant decrease in urinary sodium concentration in the hyponatraemic children treated with NS but not N/2 suggests that mechanisms other than aldosterone were acting.

We conclude that when intravenous fluids are deemed necessary in children with gastroenteritis, isotonic saline solutions with appropriate glucose content should be used. The question arises however as to whether this recommendation should be restricted to gastroenteritis. Non-osmotic stimulants of ADH secretion (such as nausea and vomiting, pain, and metabolic stress)[28] are common and likely to be active in a variety of clinical situations for which intravenous fluids are used. The protective effect of normal saline against the development of hyponatraemia and the ability of the normonatraemic children to increase urinary sodium excretion suggest that broadening the use of isotonic fluids with appropriate glucose content should be considered.

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ORIGINAL ARTICLE

Hypotonic versus isotonic saline in hospitalised children: a systematic review

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Background: The traditional recommendations which suggest that hypotonic intravenous (IV) maintenance fluids are the solutions of choice in paediatric patients have not been rigorously tested in clinical trials, and may not be appropriate for all children.
Aims: To systematically review the evidence from studies evaluating the safety of administering hypotonic versus isotonic IV maintenance fluids in hospitalised children.
Methods: Data sources: Medline (1966–2006), Embase (1980–2006), the Cochrane Library, abstract proceedings, personal files, and reference lists. Studies that compared hypotonic to isotonic maintenance solutions in children were selected. Case reports and studies in neonates or patients with a pre-existing history of hyponatraemia were excluded.
Results: Six studies met the selection criteria. A meta-analysis combining these studies showed that hypotonic solutions significantly increased the risk of developing acute hyponatraemia (OR 17.22; 95% CI 8.67 to 34.2), and resulted in greater patient morbidity.
Conclusions: The current practice of prescribing IV maintenance fluids in children is based on limited clinical experimental evidence from poorly and differently designed studies, where bias could possibly raise doubt about the results. They do not provide evidence for optimal fluid and electrolyte homoeostasis in hospitalised children. This systematic review indicates potential harm with hypotonic solutions in children, which can be anticipated and avoided with isotonic solutions. No single fluid rate or composition is ideal for all children. However, isotonic or near-isotonic solutions may be more physiological, and therefore a safer choice in the acute phase of illness and perioperative period.

Intravenous (IV) maintenance fluids are designed to provide free water and electrolyte requirements in a fasting patient. The prescription for IV maintenance fluids was originally described in 1957 by Holliday and Segar, who equated free water requirements from energy expenditure in healthy children.[1] They rationalised adding 3.0 and 2.0 mEq/100 kcal/24 h of sodium and potassium respectively, as it approximates the electrolyte requirements and urinary excretion in healthy infants.[2 3] This is the basis for the current recommendation that hypotonic IV maintenance solutions are ideal for children.[4 5] The Holliday–Segar system remains the most universally used to date, because of the simplicity of their formula. While these recommendations may be appropriate for the healthy child, they do not necessarily apply in acute illness, where energy expenditure and electrolyte requirements deviate significantly from this formula.[6]

The numbers of deaths and significant neurological sequelae from hospital acquired hyponatraemia in children receiving hypotonic maintenance solutions have increased in the past 10 years.[7–11] Several narrative reviews have suggested potential harm with these solutions and recommend that routine use in children be reconsidered.[12 13] Despite these concerns, standard texts and guidelines continue to recommend hypotonic maintenance solutions for all paediatric patients.[4 5] The objective of this systematic review was to evaluate the safety of hypotonic versus isotonic IV maintenance solutions in hospitalised children. Our secondary objective was to identify subgroups who are at greater risk of morbidity, in whom hypotonic solutions should be avoided.

METHODS

Search strategy

We searched Medline (1966–2006), Embase (1980–2006), and the Cochrane Library, using the terms: "fluid therapy", "hypotonic solution", "isotonic solution", and synonyms or related terms (Appendix 1; see http://www.archdischild.com/supplemental). We searched online (FirstSearch, Conference Proceedings) or published conference proceedings, and Current Controlled Trials (www.controlled-trials.com). Abstracts from the following 2002–05 scientific forums were hand searched: World Congress on Pediatric Intensive Care, Society for Pediatric Research, Critical Care Congress, and American Academy of Pediatrics. We reviewed the reference lists of all identified studies and reviews, and also personal files, and contacted experts and first authors to identify other published or unpublished studies.

Study selection

Citations considered potentially relevant by either of two reviewers (KC or MK) were retrieved using the following inclusion criteria:

- Controlled trials, cohort, and case-control studies. Cohort studies had to compare patients receiving hypotonic IV maintenance solutions with a control group or unexposed cohort who received isotonic solutions. Case-control studies had to compare cases, to a control group who did not have the outcomes of interest.
- Children (1 month to 17 years) hospitalised for any medical or surgical condition. We included a diverse paediatric population to capture all potential patients who currently receive "standard IV maintenance therapy".
- Intervention: currently used hypotonic and isotonic IV maintenance solutions. Solutions were classified as

Abbreviations: CI, confidence interval; ECF, extracellular fluid; IV, intravenous; PNa, plasma sodium; RCT, randomised controlled trial; WMD, weighted mean difference

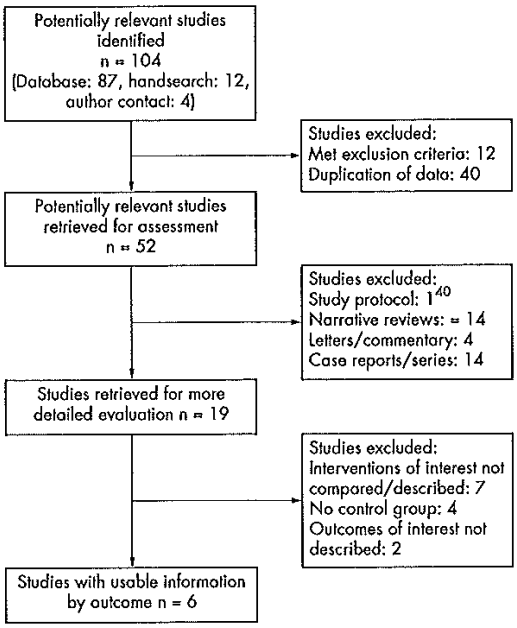

Figure 1 Flow diagram of the study selection process for this systematic review.[33]

"hypotonic" if they contained <0.9% NaCl, or "isotonic or near isotonic" (i.e. 0.9% NaCl or Ringers Lactate). We excluded case reports and studies of fluid resuscitation and oral rehydration therapy. Studies enrolling neonates, patients with pre-existing hyponatraemia and co-morbidities which result in sodium derangements (e.g. renal disease, diabetes insipidus, diuretic therapy), were also excluded.

Study outcomes

Studies were included if any of the following outcomes related to the development of acute hospital acquired plasma sodium (PNa) derangements and/or their attributed morbidity were reported: fluid balance, clinical evidence of volume overload, hypertension, seizures, cerebral oedema, death, paediatric intensive care unit admission, and length of stay. We used PNa as a surrogate outcome, as it is a convenient reflection of tonicity balance, and represents the potential for fluid shifts between intracellular and extracellular fluid (ECF) compartments. This in turn may result in clinically relevant morbidity, such as the defined outcomes of interest. A priori, we defined hyponatraemia as PNa <136 mmol/l, and severe hyponatraemia as PNa <130 mmol/l, or any level of hyponatraemia associated with symptoms. We also examined hypernatraemia since the arguments against the use of isotonic solutions in children include renal solute loading and the risk of increasing PNa. We defined hypernatraemia as PNa >145 mmol/l.

Data abstraction and study quality

In duplicate and independently, we abstracted data to describe the methodological quality and clinical characteristics of these trials. We contacted authors where necessary for additional data on outcomes of interest. We extracted the following information: study population, sample size, intervention, duration, and type of exposure and outcomes. The methodological quality of included studies was assessed using predefined criteria (Appendices 2 and 3; see http://www.archdischild.com/supplemental).

Data analysis

Cohen's Kappa statistic was used to calculate agreement between raters. For categorical outcomes, treatment effects were expressed as odds ratios (OR) and 95% confidence intervals (CI). We described treatment effects of continuous outcomes using weighted mean differences (WMD) and 95% CI. We calculated summary risk differences and 95% CI using a random effects model (RevMan Version 4.2). Where statistical pooling was not possible, we described our findings qualitatively.

RESULTS

Study selection

We identified 52 potentially relevant articles from 104 citations (fig 1); 33 did not meet inclusion criteria. Of the 19 studies retrieved for detailed evaluation, seven did not describe or compare the interventions of interest, four did not describe a control group, and two did not report any of the outcomes of interest. Six studies satisfied all criteria (table 1). Cohen's Kappa for inclusion decisions was 0.81 (almost perfect agreement).

Study characteristics

We report the characteristics of the six included studies in table 1. There were two unmasked randomised controlled trials (RCT),[14 15] and one non-randomised controlled trial.[16] Three were observational studies.[17–19] Tables 3–5 outline the study quality and methodological characteristics—the overall quality of included studies was often limited; allocation concealment, blinding of patients, clinicians, outcomes assessors, and outcomes were inconsistently or not reported across studies.

Clinical outcomes

Plasma sodium

The standard deviations (SD) were not presented for PNa in one of the studies.[14] Thus, we calculated a pooled SD to compare the PNa across studies. Hypotonic maintenance solutions significantly increased the risk of developing hyponatraemia (OR 17.22; 95% CI 8.67 to 34.2) (fig 2). Mean PNa in patients following hypotonic solutions was significantly lower (−3.39 mmol/l; 95% CI −5.35 to −1.43), than those who received isotonic solutions (fig 3). The PNa also decreased significantly greater in patients who received hypotonic solutions (−5.37 mmol/l; 95% CI −8.79 to −1.94, fig 4). None of the studies reported the development of hypernatraemia. However, three studies reported a *decrease* in PNa despite the infusion of isotonic or near-isotonic IV maintenance fluids (table 1).[15 17]

Morbidity attributed to hyponatraemia

Adverse clinical outcomes were reported in three studies.[17–19] Wilkinson reported seizures in 2/26 patients receiving hypotonic fluids (OR 6.22; 95% CI 0.29 to 135.8).[19] Hoorn reported nausea and vomiting more commonly in patients with hospital acquired hyponatraemia (68%, $p = 0.008$)[18] than isonatraemic controls. The presence of increased pulmonary interstitial fluid on chest *x* ray was reported by Burrows in 15/20 of patients receiving hypotonic solutions and 2/4 in the near-isotonic group.[20] The clinical significance of this finding was not commented on by the authors. Other outcomes of interest as listed in our objectives were not reported.

Table 1 Characteristics of included studies

	Brazel (1996)[14]	Dagli (1997)[15]	Neville (2006)[13]	Hoorn (2004)[16]	Burrows (1983)[17]	Wilkinson (1992)[19]
Participants						
n	12	60	104	148	24	56
Age (years)	12.3–18.1	1–12	6 months–14 years	7±6	6–16	2 months–14 years
Inclusion criteria	Adolescent females undergoing idiopathic scoliosis repair	ASA 1 patients undergoing elective minor surgery	Gastroenteritis with dehydration	37 patients with hospital acquired hyponatraemia, 111 isonatraemic historical controls	Previously healthy patients with idiopathic scoliosis undergoing surgical correction	Craniofacial surgery
Methodology	RCT, unmasked	Controlled trial	RCT, unmasked	Case control	Cohort study	Retrospective chart review
Intervention (all solutions included appropriate dextrose content unless otherwise stated)	Near isotonic solution (LR), n=5; v hypotonic solutions: (0.3%–0.18% NaCl), n=7	Gp 1: LR Gp 2: 1% Dextrose in LR Gp 3: 3.3% Dextrose in 0.3% NaCl	Gp1: 0.45% NaCl Gp 2: 0.9% NaCl	Standard prescription for maintenance IV fluids	Postoperative maintenance fluids: Isotonic (LR), n=4 Hypotonic (0.25–0.5% NaCl), n=20	Isotonic (LR or NS), n=30 Hypotonic (0.16–0.5% NaCl), n=26
Outcomes						
PNa mmol/l	Greater and more sustained drop in PNa in hypotonic group (p<0.01)	Post-op PNa in Gp 3 significantly lower (p<0.05). No significant change in Gp 1 and 2	Mean PNa after 4 hours: Gp 1 134.3 mmol/l (2.1) Gp 2 136.3 mmol/l (3.3)	Cases: PNa dropped from 139±3 to 133±2 mmol/l in 19±10 hours Controls: PNa 140±2 mmol/l	Greater fall in PNa in hypotonic group: 6.2±2.9 mEq/l (p<0.05); 3.0±0.8 mEq/l in isotonic group	Median PNa: 130.5 (121–136) in hypotonic Gp; 139 in isotonic group
Hyponatraemia (PNa <136)	1 patient in LR group, 7 in hypotonic group	PNa in hypotonic group (Gp 3): 133.3±4.6 mEq/l (p<0.05)	21/31 in Gp 1, 2/21 in Gp 2	All cases by definition	Post-op PNa: 131 ±2.8 in hypotonic group; 135±1.9 mmol/l in isotonic group	20/26 patients in hypotonic group, 2/30 in isotonic group
Severe hyponatraemia (PNa <130)	4 in hypotonic group	Not described	5/22 in Gp 1 (PNa <130); 0/22 in Gp 2	Not described	5 patients in hypotonic group	11 in hypotonic group
Clinical sequelae related to hyponatraemia	Not mentioned	Not described	None described	More nausea and vomiting reported in hyponatraemic group	Increased interstitial pulmonary fluid in hypotonic group (p<0.05)	Seizures: 2/26 in hypotonic group
Hypernatraemia (PNa >145)	None	None	None	None	None	None

CVS, cardiovascular; LR, Lactated Ringers; NS, normal saline; PNa, plasma sodium; pre/post-op, pre- or postoperative; Gp, group; NaCl, sodium chloride; RCT, randomised controlled trial.

Table 2 Characteristics of excluded studies

Study	Methods	Participants	Interventions	Primary outcome of study	Reason for exclusion
Neville (2005)[15]	Cohort study	Children with gastroenteritis (n = 52)	Hypotonic IV fluids	PNa; osmolality, ADH, urine electrolytes and osmolality, cortisol, and thyroid hormone	No control group
Cupido (2000)[25]	Cohort study	Post-op craniofacial patients (n = 16)	Isotonic fluid	PNa	No control group
Halberthal (2001)[30]	Retrospective chart review	Hospital acquired severe hyponatraemia within 48 h admission (n = 23).	Hypotonic fluid	Factors contributing to hospital acquired hyponatraemia	No control group
Gerick (1996)[21]	Case-control study	103 cases, 31 age matched controls	IV/PO fluid therapy	ADH and plasma renin activity in cases v controls	Outcomes of interest not described
Lavine (2001)[24]	Cohort study	Craniofacial patients (n = 10)	Isotonic IV fluid	Serum and urine electrolytes	No control group
Judd (1990)[34]	Case-control study	Tonsillectomy (n = 13)	Gp 1: perioperative NS IV fluid. GP 2: NPO, no IV fluids	Serum electrolytes, ADH, and plasma renin activity	Only one intervention of interest described
Duke (2002)[33]	RCT	Children with meningitis	Hypotonic IV fluids v moderate oral fluid restriction	Survival and neurological status	Only one intervention of interest described
Cowley (1988)[20]	Cohort study	8 healthy children undergoing scoliosis repair	Type of fluids not described individually	Serum and urine electrolytes, ADH and renin activity	Type of fluids not individually described
Arieff (1999)[26]	Retrospective chart review	Fatal cases of post-op hyponatraemia	Not described	Volume of fluid administered	Intervention not described, primarily adult study
Watad (1992)[27]	Retrospective chart review	Patients admitted with hyponatraemia	Not described	Aetiology of hyponatraemia	Interventions of interest not described
Dunn (1997)[28]	Retrospective chart review	Patients with PNa>165 or Na<130	Not described	Aetiology of hospital acquired PNa derangements	Interventions of interest not described
McCormick (1999)[29]	Retrospective chart review	Elective paediatric general surgical cases	Hypotonic or isotonic fluids	Not described	Outcomes of interest not described
Powell (1990)[32]	RCT	Children with meningitis	Fluid restriction v maintenance plus deficit replacement	PNa, plasma AVP levels	Type of fluids not individually described

ADH, antidiuretic hormone; IV, intravenous; PO, oral.

Table 3 Quality assessment; controlled trials

	Subjects			Intervention		Outcomes		Follow up		Analysis	
Author	Description of subjects	Allocation concealment	Method of randomisation described	Well defined/ objective interventions	Care taker/pt blinding	Definition	Blinding	Sufficient (≥90%)	ITT	Adjustment for confounders	Data provided to confirm results
Brazzi	Yes	No	No	Yes	No	Yes	No	Yes	No	No	Yes
Degli	Yes	No	No	Yes	No	Yes	No	Yes	No	No	Yes
Nevill	Yes	Unclear	Yes	Yes	No	No	No	Yes	No	No	Yes

Table 4 Quality assessment; observational studies—cohort studies

	Selection				Comparability	Outcome		
Author	Representativeness of exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Outcome of interest not present at start of study		Assessment	Follow up: outcomes	Follow up: cohorts
Burrows		*		*			*	*
Wilkinson		*	*			*	*	*

Table 5 Quality assessment; observational studies—case-control studies

	Selection				Comparability	Exposure		
Author	Case definition	Representativeness	Selection of controls	Definition of Controls		Ascertainment	Method of ascertainment	Non-response rate
Hoorn	*	*		*	*	*	*	*

Volume of IV fluid administration

Hoorn reported that patients with hospital acquired hyponatraemia did not receive significantly greater total fluid volume than isonatraemic patients, however the calculated electrolyte-free water intake was three times greater compared to the isonatraemic controls ($p < 0.001$). The total sodium intake in mmol/kg/h was not significantly different between the two groups.[18] The volume of IV fluid infused was not a determinant of the change in PNa at four hours in Neville's study of patients with gastroenteritis.[15] Fluid balance and volumes of fluid infused were not specifically presented in the other studies, but described as "same in both groups".

Subgroups

Four of the included studies were in surgical patients,[14 16 17 19] and one study enrolled patients with gastroenteritis.[15] Hoorn identified more surgical patients in the hospital acquired hyponatraemia group (16%), than in the isonatraemic controls (5%, $p = 0.04$).[18] All studies examined associations using univariate analyses; none used multivariate analyses to adjust for confounding factors.

Heterogeneity

Given the small number of studies, we chose to include and analyse results from both controlled trials and observational studies. Visual inspection of the Forrest plots indicated study heterogeneity; however formal statistical tests in this instance are underpowered to detect and adjust for clinically important heterogeneity, given the small number of outcomes, patients, and studies. We thus chose to describe the sources of clinical heterogeneity. (1) *Patients* included in this systematic review were heterogeneous, however the majority of studies were in the surgical population. (2) The degree of *exposure to the interventions* varied between studies—the timing of PNa measurements occurred after variable degrees and duration of exposure to intervention. (3) The majority of studies were limited in their *quality* (tables 3–5). Despite apparent heterogeneity in study design, participants, and quality among these studies, the treatment effect nevertheless appears to be remarkably consistent across the studies.

DISCUSSION

Intravenous fluids are used in children to either expand a contracted ECF space or as "maintenance" to replace urine

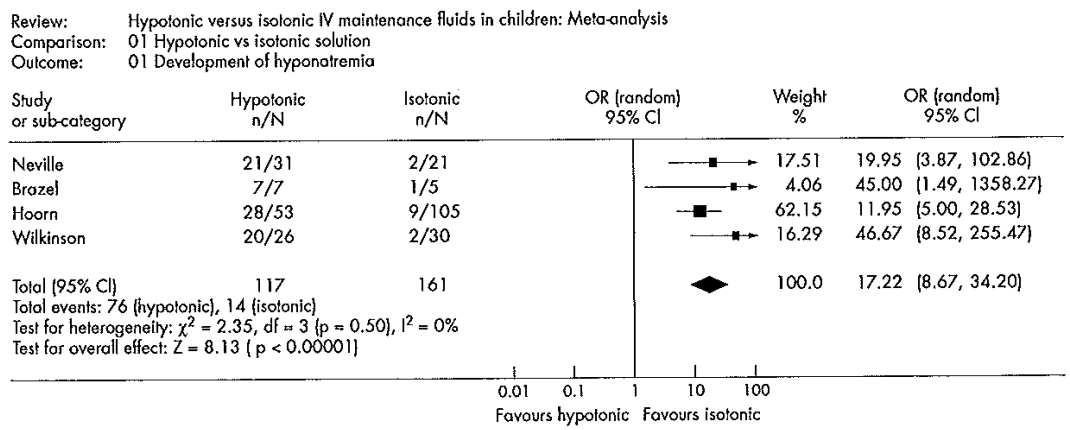

Figure 2 Forrest plot summarising the odds ratios and associated 95% confidence intervals for developing hyponatraemia in children receiving hypotonic compared to isotonic IV maintenance fluids.

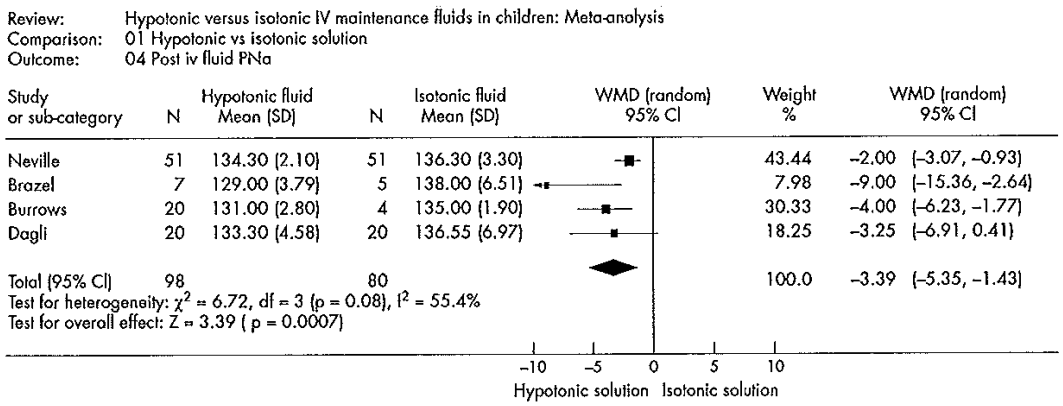

Figure 3 Comparison of PNa levels following hypotonic versus isotonic or near-isotonic IV maintenance fluids.

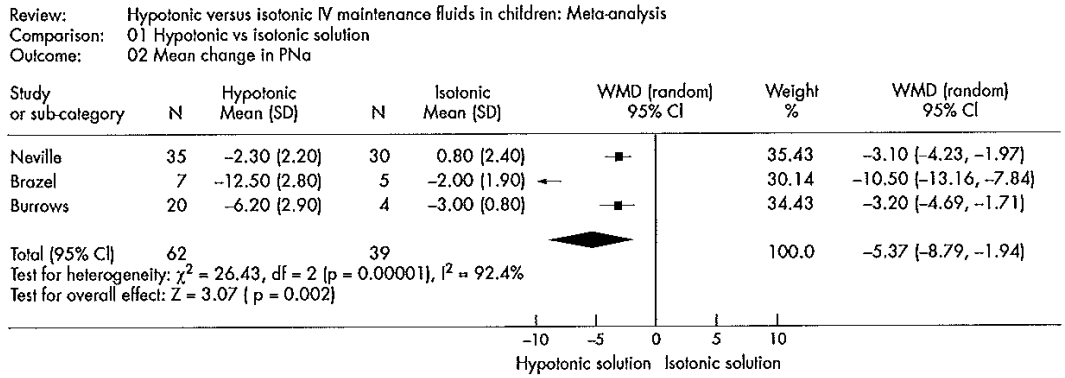

Figure 4 Mean change in PNa following hypotonic versus isotonic IV maintenance fluids.

output and insensible losses. In the former instance isotonic or near-isotonic saline is recommended on the basis that it is the physiologically appropriate solution. In the latter case hypotonic saline solutions are the accepted standard of care. This systematic review reveals that the evidence for the safety of this ubiquitous practice is limited, with only six published studies (only two of which were RCTs) reporting data on a total of 404 patients. The current level of evidence suggests that hypotonic maintenance solutions in children are not benign, but in fact potentially dangerous. The overall treatment effect is remarkable with the odds of developing hyponatraemia following hypotonic solutions being *17.2 times greater* than with isotonic fluids. Hence, there are potential risks associated with the use of hypotonic solutions in children, such as cerebral oedema precipitated by an acute fall in serum osmolality.

Hyponatraemia occurs due to a positive balance of electrolyte free water, combined with an impaired ability to excrete hypotonic urine secondary to ADH secretion. A significant correlation between free water intake and decrease in PNa has been demonstrated.[20] The primary source of electrolyte free water is the exogenous administration of hypotonic fluid. In contrast to healthy individuals, hospitalised patients have multiple non-osmotic stimuli for ADH secretion, which prevents them from producing water diuresis even in the presence of a PNa that is lower than 136 mmol/l.[12 15 21] In such patients, there will be very little if any excretion of electrolyte free water, because ADH makes the later parts of the distal nephron permeable to water.[22] The risk of hyponatraemia in these patients is under-recognised,[14 17 21] and is thus compounded by the administration of hypotonic solutions. However, the administration of isotonic maintenance solutions at least in children with meningitis, has been shown to result in a more rapid return of ADH to normal concentrations, when compared to hypotonic fluids.[23] Neville demonstrated that patients admitted with gastroenteritis have obligate urinary sodium losses irrespective of initial PNa.[15] The urinary tonicity at presentation of these patients approximates that of normal saline. Therefore infusion of a hypotonic solution which is lower in tonicity than that of urine passed is predictive of a decrease in subsequent PNa.

The concern that isotonic maintenance fluids may cause hypernatraemia is not supported in the studies we reviewed, nor is it reported in adults where the use of isotonic solutions is routine. On the contrary, the risks of hyponatraemia may also extend to patients who receive isotonic fluid.[14–16 21 24] This can be explained at least in part by the excretion of relatively hypertonic urine as demonstrated by Neville and others.[15 24 25] Steele observed that the expansion of the ECF with Ringers Lactate in the perioperative period results in the production of a hypertonic urine resulting in "desalination".[26] However,

What is already known on this topic

- The current standard of prescribing maintenance IV fluids is based on historical evidence
- The safety of this practice is yet to be tested in well conducted clinical trials

What this study adds

- This is the first systematic review which examines the evidence for standard IV maintenance solutions in children
- This review provides evidence that, at least in some paediatric patients, hypotonic solutions exacerbate the risks of hyponatraemia, while isotonic solutions may be protective

hypernatraemia can occur during the administration of isotonic saline if a hypotonic urine is produced, leading to a positive sodium balance.

The traditional guidelines for fluids in children, published 50 years ago, and more recently reiterated,[27 28] were derived from estimates of insensible water losses, and electrolyte requirements for normal growth.[1] These calculations have since been criticised, and may lead to an overestimation of hypotonic fluid requirement in sick children.[6 29] It has been demonstrated that it is not simply Na^+ intake, but moreover its ratio to electrolyte free water intake that influences PNa.[18] These findings challenge the previous recommendations made by Holliday and Segar, and argue for a maintenance solution and volume which maintains tonicity balance during acute illness, rather than one which merely provides a daily sodium or caloric requirement. We used PNa as a surrogate measure of morbidity related to fluid shifts between intra- and extracellular compartments. PNa is a convenient marker as it reflects the ratio between effective osmoles and total body water. As Na^+ is the principal extracellular cation and therefore the main determinant of ECF volume, it regulates water movement across cell membranes and explains the development of intracellular oedema that occurs in the presence of hyponatraemia. The expansion of intracellular fluid volume is of major importance in the central nervous system as the brain is confined in a rigid bony cage and has only limited ability to expand. Thus brain cell swelling is very likely to increase intracranial pressure and predispose to brain herniation. Children are at greater risk of this sequela because their brains have a larger intracellular fluid volume per total skull volume.[30] Certainly among children who develop symptomatic hyponatraemia, the incidence of permanent brain damage is substantially higher than in adults.[31]

The results of this systematic review validate the growing concerns expressed in reports which question the safety of our current practice.[13 32] The strengths of this report include a comprehensive search strategy, explicit selection criteria for relevant primary studies, reliability assessment of study screening and study quality, validity assessment of primary studies, statistical pooling of effect sizes, focus on adverse events, and reporting according to QUOROM guidelines.[33] The weaknesses are that most studies reviewed were heterogeneous in design, small, and of variable quality, did not allow for confounding factors, and focused on a limited paediatric population. Therefore we cannot state with certainty that the principles are applicable to all children prescribed IV maintenance fluids. On the other hand, we can state that, based on published case reports of deaths and neurological injury from acute hyponatraemia that the administration of hypotonic solutions to children with a PNa <138 mmol/l is potentially hazardous, given the fact that ADH is likely to be acting.

Conclusions

The current practice of prescribing IV maintenance fluids in children is not based on clinical experimental evidence using patient-important outcomes, and does not provide optimal fluid and electrolyte homeostasis in hospitalised children. There is evidence that, at least in some paediatric patients, hypotonic solutions exacerbate the risks of hyponatraemia, while isotonic solutions may be protective. Our current responsibility however, is to refrain from adopting a "new standard of care", until rigorous clinical trials comparing the safety and effectiveness of different IV fluid regimens in children have been completed.

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ORIGINAL ARTICLE

Randomised controlled trial of intravenous maintenance fluids

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Aim: Traditional paediatric intravenous maintenance fluids are prescribed using hypotonic fluids and the weight-based 4:2:1 formula for administration rate. However, this may cause hyponatraemia in sick and post-operative children. We studied the effect of two types of intravenous maintenance fluid and two administration rates on plasma sodium concentration in intensive care patients.

Methods: A Factorial-design, double-blind, randomised controlled trial was used. We randomised 50 children with normal electrolytes without hypoglycaemia who needed intravenous maintenance fluids for >12 h to 0.9% saline (normal saline) or 4% dextrose and 0.18% saline (dextrose saline), at either the traditional maintenance fluid rate or 2/3 of that rate. The main outcome measure was change in plasma sodium from admission to 12–24 h later.

Results: Fifty patients (37 surgical) were enrolled. Plasma sodium fell in all groups: mean fall 2.3 (standard deviation 4.0) mmol/L. Fluid type ($P = 0.0063$) but not rate ($P = 0.12$) was significantly associated with fall in plasma sodium. Dextrose saline produced a greater fall in plasma sodium than normal saline: difference 3.0, 95% confidence interval 0.8–5.1 mmol/L. Full maintenance rate produced a greater fall in plasma sodium than restricted rate, but the difference was small and non-significant: 1.6 (−0.7, 3.9) mmol/L. Fluid type, but not rate, remained significant after adjustment for surgical status. One patient, receiving normal saline at restricted rate, developed asymptomatic hypoglycaemia.

Conclusion: Sick and post-operative children given dextrose saline at traditional maintenance rates are at risk of hyponatraemia.

Key words: child; fluid therapy; infusion; intravenous.

Intravenous (IV) fluids have been used in paediatrics for over 50 years. The most commonly used maintenance fluid, used to replace normal expected fluid losses in situations such as fasting, is hypotonic saline with dextrose. Volumes are typically calculated using a weight-based infusion rate: for the first 10 kg, 4 mL/kg/h, for the next 10 kg, 2 mL/kg/h and 1 mL/kg/h for each kilogram thereafter.[1–6] However, it may be inappropriate for those children who have non-osmotic production of antidiuretic hormone (ADH). The syndrome of inappropriate ADH[7] occurs in meningitis,[8,9] encephalitis,[10] pneumonia,[11] bronchiolitis[12] and after surgery.[13–16] Any consequent hyponatraemia may be exacerbated by hypotonic IV fluids.[14,17]

Natriuresis (urinary salt loss) may cause hyponatraemia. Sodium loss and hypovolaemia occur in cerebral salt wasting (CSW),[18,19] probably caused by a hormone such as atrial natriuretic hormone.[19] Hyponatraemia in neurosurgical patients may be from CSW, not the syndrome of inappropriate ADH.[20] CSW occurs in children with neurological illness, neurosurgery and craniofacial surgery.[21–23]

Symptomatic hyponatraemia is uncommon if the plasma sodium ([Na]) is >120–125 mmol/L,[24,25] but depends on the rate of fall,[26] and can occur at higher values.[17] It can cause death or serious neurological morbidity.[26–28]

Recently, the prevention of hyponatraemia in hospitalised children has been debated.

Moritz and Ayus recommended isotonic maintenance fluid: 0.9% saline (NS) in 5% dextrose, instead of hypotonic fluid such as 4% dextrose and 0.18% saline (DS) or 0.45% saline, without fluid restriction.[29] Taylor and Durward recommended isotonic solutions with fluid restriction, citing small insensible losses in inactive, hospitalised children, non-osmotic ADH secretion, and increased water of oxidation.[30] Maintenance therapy for acutely ill or post-operative children is thus 50–60 mL/kg/day as NS to prevent desalination (loss of total body sodium),[13] without hypernatraemia.[31]

Others have opposed using isotonic maintenance fluid.[32] The primary cause of hyponatraemia is not desalination but dilution. Non-osmotic ADH secretion and the isotonic salt load could cause both increased total body water and over-expansion of the intravascular space. The resultant aldosterone suppression, natriuretic peptide secretion, and/or increased glomerular filtration may cause a secondary natriuresis. Hyponatraemia has developed in surgical patients receiving isotonic fluids.[13] The

Key Points

1. Children who are sick or post-operative are at risk of hyponatraemia.
2. Surgical patients may have greater falls in plasma sodium concentration than medical patients.
3. The tonicity of the fluid has a greater effect than the rate of administration

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lack of evidence for different fluid regimens justifies a randomised controlled trial, comparing both volumes and fluid types.[32] No such trial has been carried out.[33]

Five randomised controlled trials of IV fluids in children are reported. Three in children with meningitis suggested that fluid restriction was unwarranted.[34–36] None studied fluid tonicity. Some consider it unethical to give traditional maintenance fluid volumes to children with neurological and similar conditions.[37] Two other trials, one after scoliosis surgery[38] and one in gastroenteritis,[39] found that [Na] fell with hypotonic but not isotonic fluid. The former was in a select group of surgical patients and the latter was a trial of therapeutic fluid replacement in gastroenteritis – a very different situation from provision of maintenance fluid.

We carried out a factorial, randomised controlled trial comparing IV NS (isotonic) to DS (hypotonic), and the traditional versus restricted rate. The main outcome was the change in [Na] 12–24 h after admission. A second study arm compared isotonic and hypotonic fluid at restricted rates in children who would normally be fluid restricted. Because we recruited too few patients for the restricted arm, only the main arm is reported here. The main end point was the change in [Na], not neurological outcome, because detecting such a difference requires a prohibitively large sample size, and may be unethical. This outcome was a surrogate in a systematic review published after our study was conducted.[40]

Materials and Methods

Setting

The Women's and Children's Hospital is the tertiary paediatric referral centre in South Australia. The paediatric intensive care unit (PICU) has 12 beds and admits 500–550 patients annually. The hospital's research ethics committee approved the study.

Subjects

Eligible subjects were children admitted to the PICU who would normally receive IV fluid as DS at traditional maintenance rates for at least 12 h, with normal [Na] (135–145 mmol/L) and no hypoglycaemia. We classified the Australian and New Zealand Paediatric Intensive Care Registry diagnostic codes[41] into three groups: ineligible, eligible for both arms, and eligible only for the restricted arm. We excluded neonates, and those with diabetes, renal failure or shock. Conditions eligible only for the restricted arm included cardiac and neurosurgical patients. A list of ineligible and restricted fluid conditions is available from the authors.

We obtained written, informed consent from the parents or the patient. They were approached as soon as possible after PICU admission, once the initial [Na] and blood glucose were known, and before starting maintenance IV fluids.

Study fluids

Study fluids were prepared by non-clinical staff, using standard solutions and covering the bags with black plastic. The bags were put into sealed, numbered boxes. All clinical staff were blinded to the fluid type, but not rate. A code was kept in the pharmacy enabling unmasking if needed. Any additives were injected through the usual port without identifying the fluid.

Randomisation was by random numbers using blocks of six. Enrolled patients were assigned consecutive study numbers from a list, and received the corresponding numbered box containing study fluid, with the administration rate specified as 'maintenance' or 'restricted' inside the box, invisible until the box was opened.

For those randomised to the 'maintenance' group, the study fluid was administered at the standard, maintenance fluid rate.[1] Additional fluid boluses were permitted, as NS, if clinically indicated. Oral fluids were allowed and recorded. The 'restricted' fluid group received two-thirds of the standard rate. The treating physicians determined all other management.

We measured the plasma and urine electrolytes and osmolality on PICU admission and 12–24 h later as is our usual practice. [Na] was measured with an indirect ion selective electrode using the Beckman Coulter Synchron CX5 (Beckman Coulter, Fullerton, CA, USA). Fluid balance was documented from admission until the study period ended, when the second blood sample was taken. Other data included post-operative status, demographic data, diuretic use and whether ventilated.

The main outcome was the difference in change in [Na] for either comparison (type of fluid, and infusion rate) at 12–24 h. Secondary outcomes included change in osmolality, need for additional fluid boluses and adverse events including neurological complications, for example, seizures or headaches, and dehydration or shock.

Sample size and statistics

From previous data, the mean fall in [Na] over the first 12–24 h was 3.1 mmol/L, with a standard deviation of 4.41 mmol/L. We estimated a total sample size of 48 (12 per group) to detect a difference of 5 mmol/L, with an alpha of 0.01 and 90% power. An increase of 5 mmol/L is the suggested aim when treating symptomatic hyponatraemia.[42]

We compared both fluid type and administration rate using two-way ANOVA. For continuous data, we used Student's *t*-test and non-parametric tests as appropriate. Categorical data were analysed using Fisher's exact test. STATA version 9.2[43] was used. No adjustment was made for multiple comparisons. We could not analyse by intention-to-treat because three subjects lacked final [Na] data. All subjects received their assigned study fluid.

Results

Between 14 March and 2 November 2005 there were 332 PICU admissions, of which 53 subjects were enrolled. The reasons for exclusion are shown in Table 1. Three subjects did not have [Na] data for analysis, and were excluded. One patient was withdrawn at the parents' request because of hyperglycaemia (19.4 mmol/L) after 7 h of study fluid (DS at full maintenance rate). Two lacked final laboratory measurements owing to an oversight (NS, restricted), and early PICU discharge (NS, full). Therefore, there were 50 subjects with analysable data.

Baseline demographics and biochemistry, fluid data and change in biochemistry are shown in Tables 2–5, respectively.

Table 1 Reasons for exclusion

Reason for exclusion	*n*	%
Diagnosis an exclusion criterion	42	16
Not approached	69	26
Previous enrolment	10	4
Refused consent	13	5
Neonate <29 days old	29	11
Contraindication to study fluids	9	3
No IV *in situ*	2	1
No IV fluid indicated, e.g. fed enterally	58	22
Abnormal plasma Na concentration	7	3
Abnormal plasma glucose concentration	1	0
Other e.g. short (<12 h) stay	28	10
Total	268	100

Overall, [Na] decreased by a mean of 2.3 (standard deviation (SD) 4.0) mmol/L. Because of a preponderance of bigger subjects in group 2 (Table 4) we calculated fluid intakes per square metre body surface area, using a formula based on weight.[44] Change in [Na] satisfied the assumptions of ANOVA, including normality and homogeneity of variances. Fluid type significantly affected the fall in [Na]. The change in [Na] was significantly affected by fluid type ($P = 0.0063$) but not rate ($P = 0.12$) without an interaction between fluid type and rate ($P = 0.79$). Because there were only two fluid groups and no interaction, we compared them with *t*-tests to estimate confidence intervals: DS produced a greater mean fall in [Na] of 3.0 (0.8, 5.1) mmol/L compared with NS. Full maintenance rate produced a greater mean fall of 1.6 (−0.7, 3.9) mmol/L, compared with the restricted rate. One subject (DS, restricted) received furosemide, but omitting that subject did not change the results. Three subjects received non-study fluid, ranging from 9 to 27 mL/kg, after their first [Na] measurement. Omitting them made no difference to the results.

However, when the subjects were categorised for infusion duration above and below 15 h, the median only subjects with longer infusions (14 NS, 13 DS) showed an effect of fluid type: the mean difference was 4.1 (0.75, 7.5) mmol/L, $P = 0.019$. For subjects with shorter infusions (10 NS, 13 DS), the mean difference was 1.8 (−0.97, 4.5) mmol/L, $P = 0.19$. Infusion rate had no effect, regardless of duration (data not shown).

There was no difference in the proportion of subjects receiving fluid boluses (Table 4; Fisher's exact test $P = 0.89$). However, surgical patients were more likely to receive boluses, 22/37 (55%), than medical patients, 3/13 (23%), $P = 0.051$. Surgical patients received a greater median total volume of fluid boluses: 10 (interquartile range 0–20) versus 0 (0–0) mL/kg, $P = 0.006$ (Wilcoxon rank-sum test). There were no differences in the volume of boluses received between the two fluid types and the two rates.

In exploratory analyses, we compared and adjusted for surgery and ventilation. Surgical subjects had a greater fall in mean [Na] of 2.9 (SD 3.9) mmol/L than medical patients: 0.6 (SD 3.0), difference 2.3 (−0.1, 4.6) mmol/L, $P = 0.057$. Surgery was a significant covariate in the model comparing fluid type and rate for change in [Na] ($P = 0.002$), as was fluid type ($P < 0.001$), but not rate ($P = 0.13$). Among surgical patients, there were significantly greater falls in mean [Na] for DS compared with NS: 4.4 (1.9, 6.8) mmol/L, $P = 0.0009$. There were no significant differences between treatments for the 13 medical subjects. Mechanical ventilation made no difference to fall in [Na]: 2.1 (SD 4.1) and 2.8 (SD 4.0) mmol/L for ventilated and non-ventilated patients, respectively.

Findings for osmolality were similar to those for [Na].

There were no differences among groups for urine output. There were no statistically significant differences in final, or change in, urinary [Na]. Surgical patients tended to have greater increases in urinary sodium: mean difference 50 (49, 149) mmol/L ($P = 0.32$).

Two subjects had adverse events. One developed hyperglycaemia, described earlier as a withdrawal. The other was a 10-month-old, ex-premature child recovering from craniofacial surgery with asymptomatic hypoglycaemia, receiving NS at restricted rate. The blood glucose was 1.0 mmol/L, detected on the second scheduled sample. IV dextrose normalised the blood glucose.

Discussion

In this factorial, randomised controlled trial of maintenance fluids in children in ICU, we found that the type of fluid has a greater effect on [Na] concentration than its administration rate. However, we cannot exclude a smaller but important effect of administration rate. Most patients were surgical, mildly ill and not ventilated. Surgical patients had greater falls in [Na] concentration than medical patients.

The strengths of our study were as follows. First, because of the controversy between the 'dilutional'[32,45] versus 'desalination'[12,13,20,29] hypotheses, we compared both different fluid administration rates and types of fluid. Second, we conducted a randomised controlled trial with allocation concealment and blinding. Finally, although we used a surrogate marker for adverse events, hyponatraemia, this marker is considered the most important predictor of adverse events from fluid prescription.[26–28] This study is the only randomised controlled trial of maintenance fluid replacement in a general paediatric ICU population may still inform clinicians prescribing IV maintenance fluids.

The weaknesses were as follows. First, the duration was short and variable: children were only followed for 12–24 h, and while this may represent a common situation of an overnight fast we cannot extrapolate the findings to later effects on electrolytes. Furthermore, within this short time, the duration of infusion had an effect, with only longer infusions producing a statistically significant fall in [Na]. ADH effect peaks around 24 h post operation,[38,46] but can occur as early as 5–17.5 h post operation in children.[47] Second, contamination by non-study and anaesthetic fluids might have affected the results. The percentage of fluid received as study fluid ranged between 61% and 79%, but we did not record fluids received before ICU admission. This should have been accounted for by randomisation, and we have shown that the fluid prescribed post-operatively affects [Na]. Third, because of the small sample, there was a chance imbalance in patient size between groups, with group 2

Table 2 Baseline characteristics by fluid type and rate

Group	1 NS restricted	2 NS full	3 DS restricted	4 DS full
n	13	11	15	11
Surgical, *n* (%)	11 (84)	10 (91)	8 (53)	8 (72)
Craniofacial surgery, *n* (%)	4 (31)	3 (27)	4 (27)	4 (36)
Spinal surgery, *n* (%)	4 (31)	7 (64)	2 (13)	1 (9)
Age (years), median (IQR)	5.3 (0.9, 12)	15.4 (10.8, 15.9)	4.7 (1.4, 8.9)	3.7 (1.5, 14.7)
Weight (kg), median (IQR)	17 (8, 36)	44 (26, 75)	15 (8.9, 22)	13 (10, 39)
PIM2 risk of death (%), median (IQR)	0.5 (0.2, 0.9)	0.2 (0.1, 0.5)	0.3 (0.1, 1.0)	1.9 (0.4, 3.2)
Ventilated, *n* (%)	3 (23)	1 (9)	4 (27)	7 (64)

IQR, interquartile range; DS, 0.18% saline; NS, 0.9% saline; *n*, number in group.

Table 3 Baseline biochemistry, mean (standard deviation) by fluid type and rate

Group	1 NS restricted	2 NS full	3 DS restricted	4 DS full
n	13	11	15	11
Na (mmol/L)	140 (2)	141 (2)	141 (2)	141 (3)
K (mmol/L)	4.2 (0.3)	4.1 (0.6)	4.1 (0.6)	4.8 (1.7)
Cl (mmol/L)	108 (4)	109 (3)	107 (5)	108 (5.5)
Urea (mmol/L)	4.3 (1.2)	4.2 (1.4)	5.3 (3.8)	4.9 (1.5)
Creatinine (mmol/L)	0.05 (0.02)	0.05 (0.02)	0.04 (0.01)	0.05 (0.03)
Bicarbonate (mmol/L)	22.8 (3.7)	22.7 (3.3)	20.8 (2.5)	21.9 (5.6)
Osmolality (mosm/kg)	298 (18)	299 (11)	298 (8)	299 (16)
Urine Na (mmol/L)	80 (72)	64 (45)	99 (71)	96 (60)
Urine K (mmol/L)	86 (37)	57 (36)	81 (49)	88 (37)
Urine Osmolality (mosm/kg)	571 (213)	451 (156)	639 (280)	580 (155)

Three had missing data for osmolality (one restricted rate, NS; one full rate, NS; one restricted rate, DS). Four subjects were missing data for urinary chemistry (two restricted rate, DS, one full rate, NS and one full rate, DS). DS, 0.18% saline; NS, 0.9% saline; *n*, number in group.

(NS, full maintenance rate) having larger, older children. Because of the non-linear formula for maintenance fluids, that group received less fluid per kilogram than other groups. Fourth, we did not power the study to detect fluid overload and we did not measure weight or sodium balance. Although there were no clinically apparent adverse effects, we excluded children at risk such as cardiac patients. Fifth, we did not study neurological outcomes for practical and ethical reasons. Finally, our sample was a relatively well ICU population, better reflecting post-operative and mildly ill children than the general ICU population.

Our results echo those from other non-meningitis controlled trials and a recent systematic review.[40] Brazel and McPhee randomised adolescent girls undergoing correction of scoliosis to near-isotonic or hypotonic fluid, in an unmasked study.[38] [Na] fell more in the hypotonic group. Recently, Neville *et al.* in a randomised unmasked study compared IV rapid replacement fluids in children with gastroenteritis.[39] Hypotonic fluid (0.45% saline 2.5% dextrose) reduced [Na] at 4 h but NS increased [Na]. Among normonatremic children ([Na] > 134 mmmol/L), hypotonic fluid reduced [Na] by 2.3 (SD 2.2) mmol/L, but NS increased [Na] by 0.8 (SD 2.4) mmol/L. Rate of administration made no difference, but was not randomised.

The mechanism by which fluid tonicity had a greater effect than administration rate is unclear because we did not measure regulatory hormones, extracellular fluid volume or weight. Nevertheless, our results do not support the hypothesis that high levels of non-osmotic ADH cause hyponatraemia regardless of fluid type. Potential future studies include comparing two rates of isotonic fluids with a larger sample, studies of 0.45% saline 5% dextrose and studies in different populations, for example sicker children and cardiac surgical patients. Longer follow-up, measurement of ADH and regulatory hormones, stratification to avoid chance imbalances for size and surgery, stricter protocols for non-study fluids and measurement of anaesthetic fluids should be considered.

In practice, we would not recommend using DS, 4% dextrose and 0.18% saline; NS, 0.9% saline at traditional maintenance rates in sick or post-operative children.

Table 4 Fluid volumes by group

Group	1 (NS restricted)	2 (NS full)	3 (DS restricted)	4 (DS full)
Total fluid intake (mL/kg)	45 (37, 59)	49 (36, 79)	51 (34, 68)	55 (48, 71)
Total fluid intake (mL/m^2)	1108 (881, 1196)	1294 (978, 1653)	973 (841, 1535)	1354 (1177, 1507)
Total fluid intake (mL/kg/h)	2.5 (2.2, 4.1)	3.4 (1.9, 3.7)	2.6 (2.1, 4.9)	4.1 (3.7, 4.5)
Study fluid intake (mL/kg)	29 (24, 36)	29 (23, 32)	34 (30, 42)	44 (25, 61)
Study fluid intake (mL/m^2)	662 (568, 848)	780 (620, 896)	758 (655, 928)	999 (666, 1230)
Study fluid intake (mL/kg/h)	2.0 (1.4, 2.6)	1.9 (1.5, 2.1)	2.2 (1.6, 2.6)	3.1 (2.4, 3.9)
% fluid as study fluid	64 (55, 79)	61 (51, 80)	78 (61, 88)	79 (66, 84)
Fluid bolus *n* (%) of subjects	7 (54)	6 (55)	6 (40)	6 (55)
Fluid boluses (mL/kg)	4.5 (0, 7.7)	10.7 (0, 19.7)	0 (0, 15.3)	10 (0, 17.7)
Duration of study fluid infusion (h)	16.7 (3.5)	15.4 (2.7)	16.4 (3.9)	14.1 (3.5)
Total fluid output (mL/kg)	23 (18, 29)	19 (12, 25)	21 (18, 46)	19 (14, 31)
Fluid balance (mL/kg)	31 (26)	36 (29)	25 (25)	39 (22)
Urine output (mL/kg/h)	1.2 (1.0, 1.4)	1.1 (0.8, 1.6)	1.4 (0.6, 2.3)	1.2 (0.8, 1.2)

Data are expressed as mean (standard deviation) or median (interquartile range) where appropriate. DS, 0.18% saline; NS, 0.9% saline.

Table 5 Change in electrolyte concentrations, mean (standard deviation), for subjects with complete data for initial and final electrolytes

Group	1 (NS restricted)	2 (NS full)	3 (DS restricted)	4 (DS full)
n	13	11	15	11
Na (mmol/L)	−0.2 (3.5)	−1.5 (4.3)	−3 (3.3)	−4.9 (4.0)
K (mmol/L)	0.01 (0.6)	0.21 (0.85)	−0.27 (0.57)	−0.63 (1.87)
Cl (mmol/L)	−0.2 (3.3)	−0.4 (3)	−3.1 (3.7)	−4.3 (2.3)
Urea (mmol/L)	0.25 (1.48)	0.11 (0.98)	−2.0 (5.03)	−0.75 (1.31)
Creatinine (mmol/L)	−0.003 (0.016)	−0.008 (0.011)	0.001 (0.014)	−0.009 (0.016)
Bicarbonate (mmol/L)	−1 (2.5)	−0.8 (1.8)	1.4 (2.3)	1.5 (3.5)
Osmolality (mosm/kg)	−4.9 (14.8)	−5.4 (12.1)	−11.7 (9.1)	−14.9 (11.5)
Urine Na (mmol/L)	86 (69)	117 (72)	1 (89)	78 (270)
Urine K (mmol/L)	−8.2 (41)	32.4 (49)	−14 (29)	−3.6 (55)
Urine Osmolality (mosm/kg)	318 (268)	438 (233)	3 (266)	133 (264)

Two subjects had missing data for final glucose (full rate, one NS and one DS). One subject had missing data for final osmolality (restricted rate, DS). One subject had missing data for final urinary chemistry (restricted rate, DS). DS, 0.18% saline; NS, 0.9% saline.

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TABLE 21.5.
Indications for Airway Mangement in the Child

Abnormalities of respiratory rate and rhythm
Upper airway obstruction
Loss of pharyngeal muscle activity and tone
Inability to clear secretions
Foreign body
Direct trauma
Seizures
Loss of protective airway reflexes
Pulmonary disease
Failure of oxygenation
Failure of ventilation
Pulmonary hypertension
Respiratory muscle dysfunction
Fatigue
Shock states
Secondary to nerve dysfunction
Chest wall dysfunction
Intracranial hypertension
Prophylactic

TABLE 21.6.
Summary of Drugs and Doses

Thiopental—0.5 mg per kilogram i.v., 2.5–4.5 mg per kilogram (per adequate blood pressure)
Atropine—0.01–0.03 mg per kilogram (minimum 0.15 mg)
Succinylcholine—1.0–1.5 mg per kilogram
Pancuronium—0.01 mg per kilogram (defasciculating dose); 0.1 ml per kilogram (paralysis dose, 1–2 hr)

drug usage are discussed thoroughly in Chapter 3. In general the following guidelines are used. Thiopental is administered intravenously for sedation and to blunt the observed elevation in ICP in repsonse to tube replacement. Thiopental should be used only if the systemic blood pressure is adequate. The recommended dosage is 0.5 mg per kilogram intravenously. If no systemic hypotension occurs, doses as high as 2.5 to 4.5 mg per kilogram may be used. Lidocaine may be used as an alternative to thiopental. This is primarily to blunt the ICP response to intubation and may be given via the endotracheal tube or intravenously. The recommended dosage is 1 mg per kilogram. Atropine is used to control oral tracheal secretions but more importantly to block vagal responses to succinylcholine and endotracheal tube placement. The recommended dosage is 0.01 to 0.03 mg per kilogram, with a minimum dose of 0.15 mg. Muscle relaxation is obtained by using succinylcholine. Succinylcholine is contraindicated in ocular injuries. It must be noted that succinylcholine may cause muscle fasciculations and it may affect the ICP adversely. This can be prevented by administering pancuronium initially. Pancuronium may also be used for muscle relaxation. The recommended dose of succinylcholine is 1.0 to 1.5 mg per kilogram. The recommended dose of pancuronium is 0.01 mg per kilogram for defasciculation as a pretreatment to succinylcholine use or 0.1 ml per kilogram to be used for muscle relaxation in lieu of succinylcholine. At this dosage however, paralysis may persist for 1 to 2 hr.

During the intubation it must be assumed that the patient has eaten recently, so further gastric distention must be avoided. This goal is achieved in two ways. The first is the avoidance of prolonged mask ventilation, which predisposes to further gastric distention and possible aspiration. The second is achieved by performing Sellick's maneuver, which is esophageal compression. This aids in the prevention of reflux and subsequent aspiration. Thus if the patient is breathing spontaneously, oxygenation is obtained by holding a face mask with 100% O_2 on the patient's face for 2 min. This is followed by the administration of drugs, Sellick's maneuver, and endotracheal intubation of the patient. If the patient is not breathing spontaneously, Sellick's maneuver is performed, and the drugs are administered. Simultaneously, the patient is preoxygenated with the administration of 100% O_2 by face mask, with use of about five artificial ventilations. This is immediately followed by intubation. These guidelines are useful to ensure a successful intubation with minimal trauma and complications.

After successful intubation, the position of the tube should be checked on chest X-ray. The ideal location is 2 cm above the carina. The head should be in a neutral position at the time of chest X-ray, as the position of the tube will change with changing position of the head.

Fiberoptic and/or nasotracheal intubation may need to be utilized in difficult or impossible oral intubations. These should only be considered with appropriate personnel and equipment.

Ventilation

Once the airway has been established, the patient must be ventilated. Even in relatively stable patients who are closely monitored, intermittent episodes of hypoventilation can occur. Also in small children, exhaustion of pulmonary musculature is frequently seen (84). Both of these adverse events are minimized by mechanical ventilation. In the head-injured patient, hypercarbia must be avoided. Carbon dioxide is a very potent cerebral vasodilator, and the resultant increase in cerebral blood volume may have deleterious effects on ICP and overall neurological outcome. Thus in head-injured patients requiring mechanical ventilation, hyperventilation is used with PCO_2 kept within a range of 25 to 30 torr. Immediate improvement in the EEG and overall improved outcome are seen (85, 86). The immediate physiological response to hyperventilation and relative hypocarbia include diminished cerebral blood flow with diminished cerebral blood volume, a

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used in children with pulmonary edema, chronic lung disease, or liver disease. Paraldehyde has been reported to cause pulmonary hemorrhage, pulmonary edema, acidosis, hepatitis, nephrosis, and bleeding diatheses (49).

Several other anticonvulsants may be considered if patients do not respond to previous agents. *Valproic acid* is not available in parenteral form, but has been used rectally for the treatment of status epilepticus (50, 51). A major disadvantage is its relative slowness in absorption compared to drugs that are administered intravenously. *Lidocaine* (50 to 100 mg bolus in adults) may be effective in some persons when other drugs have failed (49, 52), but higher doses of this drug are epileptogenic, and its use is not advocated in children. *Clonazepam* (53) and *chlormethiazole* (49) also have been used in status epilepticus with some success, but they have not gained widespread acceptance, particularly for use in children.

In view of the potential morbidity and mortality associated with generalized tonic-clonic status epilepticus, numerous authors have recommended the use of *general anesthesia* or barbiturate coma to minimize the metabolic sequelae of prolonged seizure activity or to suppress the process permanently (54–57). Few guidelines exist regarding the depth or duration of anesthesia or the advantages of inhalation anesthesia (56) versus intravenous agents (48), and use of anesthesia for this purpose is not universally accepted (58). With general anesthesia, with or without neuromuscular blockade, the motor manifestations of status are clearly masked. However, electrical activity may persist, and EEG monitoring is helpful during such therapy (57). In addition, convulsion-like activity on the EEG may be provoked with general anesthesia utilizing halothane, enflurane, or etomidate. The anesthetic must be periodically decreased to determine whether continued therapy is required. Despite the controversy about this modality of therapy, the experimental physiologic data concerning status epilepticus support aggressive therapy and suggest that the most severe, refractory patients be considered for general anesthesia or barbiturate coma to stop the seizures.

FURTHER EVALUATION

Although the control of seizures is of utmost importance, evaluation of their etiology should be initiated within the first few minutes after the patient is seen. Laboratory tests should include determination of serum electrolytes, glucose, calcium, hepatic enzymes, urea nitrogen, and when indicated, a toxicology screen and serum magnesium. A Dextrostix test performed at bedside can be an immediate clue to ruling out hypoglycemia. If the patient is known to have epilepsy, serum anticonvulsant levels should be measured. If meningitis is suspected, a lumbar puncture should be carried out when the child is stabilized. Evidence of increased intracranial pressure or a focal neurologic examination mandates consideration of computerized axial tomography scanning or other neurologic studies as soon as possible.

SUMMARY

Status epilepticus causes significant mortality and morbidity and must be regarded as a medical emergency. The longer the seizures are permitted to continue, the more difficult they become to control, and the worse the prognosis. It is not surprising that this is true in view of the laboratory evidence reviewed earlier in this chapter. What is surprising is that some physicians continue to tolerate periods of status epilepticus that are much longer than ought to be permitted. Delayed treatment disregards an enormous amount of pathologic evidence that status epilepticus, per se, is harmful to the CNS. Immediate, rational, and potentially aggressive therapy is essential to reduce the mortality and long-term morbidity of status epilepticus.

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