BRIEF FOR EXPERT ON NEUROPATHOLOGY
ADAM STRAIN

Introduction

1. Adam Strain is one of 4 children who are the subject of a public inquiry being conducted by John O'Hara QC.

2. Adam was born on 4th August 1991. He died on 28th November 1995 in the Royal Belfast Hospital for Sick Children ("the Royal") following kidney transplant surgery. The Inquest into his death was conducted on 18th and 21st June 1996 by John Leckey the Coroner for Greater Belfast, who engaged as experts: (i) Dr. Edward Sumner then Consultant Paediatric Anaesthetist at Great Ormond Street Hospital for Sick Children ("Great Ormond Street"); (ii) Dr. John Alexander Consultant Anaesthetist at Belfast City Hospital; and (iii) Professor Peter Berry of the Department of Paediatric Pathology in St. Michael's Hospital, Bristol. The Inquest Verdict identified Cerebral Oedema as the cause of his death with Dilutional Hyponatraemia as a contributory factor.

3. The other 3 children are :

   (1) Claire Roberts was born on 10th January 1987. She was admitted to the Royal on 21st October 1996 with a history of malaise, vomiting and drowsiness and she died on 23rd October 1996. Her medical certificate recorded the cause of her death as Cerebral Oedema and Status Epilepticus. That certification was subsequently challenged after a television documentary into the deaths of Adam and 2 other children (Lucy Crawford and Raychel Ferguson).

   The Inquest into Claire's death was carried out by John Leckey on 4th May 2006 who engaged as experts Dr. Robert Bingham (Consultant Paediatric Anaesthetist at Great Ormond Street) and Dr. Ian Maconochie (Consultant in Paediatric A&E Medicine at St Mary's, London). The Inquest Verdict found the cause of Claire's death to be Cerebral Oedema with Hyponatraemia as a contributory factor.

   (2) Raychel Ferguson was born on 4th February 1992. She was admitted to the Altnagelvin Area Hospital on 7th June 2001 with suspected appendicitis. An appendectomy was performed on 8th June 2001. She was transferred to the Royal on 9th June 2001 where brain stem tests were shown to be negative and she was pronounced dead on 10th June 2001. The Autopsy Report dated 11th June 2001 concluded that the cause of her death was Cerebral Oedema caused by Hyponatraemia.

The Inquest into Raychel's death was conducted on 5th February 2003 by John Leckey who once more engaged Dr. Edward Sumner as an expert. The Inquest Verdict found the cause of Raychel's death to be Cerebral Oedema with Acute Dilutional Hyponatraemia as a contributory factor. It also made findings that the Hyponatraemia was caused by a combination of inadequate electrolyte replacement following severe post-operative vomiting and water retention resulting from the secretion of anti-diuretic hormone (ADH).

(3) Conor Mitchell was born on 12th October 1987 with cerebral palsy. He was admitted to A&E Craigavon Hospital on 8th May 2003 with signs of dehydration and for observation. He was transferred to the Royal on 9th May 2003 where brain stem tests were shown to be negative and he was pronounced dead on 12th May 2003.

The Inquest into Conor's death was conducted on 9th June 2004 by John Leckey, Coroner who again engaged Dr. Edward Sumner as an expert. Despite the Inquest, the precise cause of Conor's death remains unclear.

The clinical diagnosis of Dr. Janice Bothwell (Paediatric Consultant) at the Royal was brainstem dysfunction with Cerebral Oedema related to viral illness, over-rehydration/inappropriate fluid management and status epilepticus causing hypoxia. Dr. Brian Herron from the Department of Neuropathy, Institute of Pathology, Belfast performed the autopsy. He was unsure what 'sparked off' the seizure activity and the extent to which it contributed to the swelling of Conor's brain but he considered that the major hypernatraemia occurred after brainstem death and therefore probably played no part in the cause of the brain swelling. He concluded that the ultimate cause of death was Cerebral Oedema. Dr. Edward Sumner commented in his Report of November 2003 that Conor died of the acute effects of cerebral swelling which caused coning and brainstem death but he remained uncertain why. He noted that the volume of intravenous fluids was not excessive and the type appropriate but queried the initial rate of administration. That query was raised in his correspondence shortly after the Inquest Verdict. In that correspondence, Dr. Sumner described the fluid management regime as 'sub-optimal'.

The Inquest Verdict stated the cause of death to be Brainstem Failure with Cerebral Oedema, Hypoxia, Ischemia, Seizures and Infarction and Cerebral Palsy as contributing factors.

4. The impetus for this Inquiry was a UTV Live 'Insight' documentary 'When Hospitals Kill' shown on 21st October 2004. The documentary primarily focused on the death of a toddler called Lucy Crawford (who died in hospital in 2000 and whose death was subsequently found to have been as a result of hyponatraemia). The programme makers identified what they considered to

have been significant shortcomings of personnel at the Erne Hospital where Lucy had been initially treated before being transferred to the RBHSC. In effect, the programme alleged a cover-up and it criticised the hospital, the Trust and the Chief Medical Officer. The programme also referred to the deaths of Adam and Raychel in which hyponatraemia had similarly played a part. At that time, no connection had been made with the deaths of Claire and Conor.

Original Terms of Reference

5. The Inquiry was established under the Health and Personal Social Services (Northern Ireland) Order 1972, by virtue of the powers conferred on the Department by Article 54 and Schedule 8 and it continues pursuant to the Inquiries Act 2005.

6. The original Terms of Reference for the Inquiry as published on 1st November 2004 by Angela Smith (then Minister with responsibility for the Department of Health, Social Services and Public Safety) were:

> "To hold an Inquiry into the events surrounding and following the deaths of Adam Strain, Lucy Crawford and Raychel Ferguson, with particular reference to:
>
> i. The care and treatment of Adam Strain, Lucy Crawford and Raychel Ferguson, especially in relation to the management of fluid balance and the choice and administration of intravenous fluids in each case.
> ii. The actions of the statutory authorities, other organisations and responsible individuals concerned in the procedures, investigations and events which followed the deaths of Adam Strain, Lucy Crawford and Raychel Ferguson.
> iii. The communications with, and explanations given to, the respective families and others by the relevant authorities.
>
> In addition, Mr O'Hara will:
>
> (a) Report by 1 June 2005 or such other date as may be agreed with the Department, on the areas specifically identified above and, at his discretion, examine and report on any other relevant matters which arise in connection with the Inquiry.
>
> (b) Make such recommendations to the Department of Health, Social Services and Public Safety as he considers necessary and appropriate."

Changes

7. There have been a number of significant changes in the Inquiry since 2005. Firstly, following representations from the Crawford family who wished to have Lucy excluded from the Inquiry's work, the Inquiry received the following Revised Terms of Reference from the Minister:

> "1. The care and treatment of Adam Strain and Raychel Ferguson, especially in relation to the management of fluid balance and the choice and administration of intravenous fluids in each case.
>
> 2. The actions of the statutory authorities, other organisations and responsible individuals concerned in the procedures, investigations and events which followed the deaths of Adam Strain and Raychel Ferguson.
> 3. The communications with and explanations given to the respective families and others by the relevant authorities.
>
> In addition, Mr O'Hara will:
> (a) Report by 1 June 2005 or such date as may be agreed with the Department, on the areas specifically identified above and, at his discretion, examine and report on any other matters which arise in connection with the Inquiry.
> (b) Make such recommendations to the Department of Health, Social services and Public Safety as he considers necessary and appropriate."

8. Secondly, Claire Roberts and Conor Mitchell were included into the Inquiry's work by the Chairman. In Claire's case that decision arose out of the belated acknowledgement by the RBHSC that hyponatraemia played a part in Claire's death. In Conor's case the decision arose out of apparent fluid mismanagement in his care soon after the implementation of Guidelines on Hyponatraemia that stressed the importance of fluid management.

9. The effect of the Revised Terms of Reference was to exclude all explicit references to Lucy Crawford. The Chairman has interpreted them in the following way:

> "... the terms still permit and indeed require an investigation into the events which followed Lucy's death such as the failure to identify the correct cause of death and the alleged Sperrin Lakeland cover-up because they contributed, arguably, to the death of Raychel in Altnagelvin. This reflects the contention that had the circumstances of Lucy's death been identified correctly and had lessons been learned from the way in which fluids were administered to her, defective fluid management would not have occurred so soon afterwards (only 14 months later) in Altnagelvin, a hospital within the same Western Health and Social Services Board area."

10. Claire Robert's case is being investigated in accordance with precisely the same terms as those of Adam Strain and Raychel Ferguson.

11. The investigation of Conor will address more limited issues in view of the fact that hyponatraemia was not thought to be a cause of his death (indeed if anything he developed hypernatraemia). Similarly, the fluid mismanagement referred to by Dr. Sumner was not considered to have been a cause of his death. So far as Conor's death is concerned, the Chairman has stated:

> "It is obviously a matter of concern if guidelines which have been introduced as a result of a previous death or deaths and which are aimed at avoiding similar events in the future, are not properly communicated to hospital staff and followed. It is relevant to the investigation to be conducted by the Inquiry whether and to what extent the guidelines had been disseminated and followed in the period since they were published. Another matter of

interest is whether the fact that Conor was being treated on an adult ward rather than a children's ward made any difference to the way in which it appears that the guidelines may not have been followed.

Accordingly, the Inquiry will investigate the way in which the guidelines had been circulated by the Department, the way in which they had been made known to hospital staff and the steps, if any, which had been taken to ensure that they were being followed. While this is an issue of general importance, it will be informed by an examination of the way in which the guidelines had been introduced and followed in Craigavon Area Hospital by May 2003."

Role of the Experts

12. The Role of the Experts to the Inquiry is set out in 'Protocol No.4: Experts', a copy of which is attached. There are 4 categories of expert assistance:

    (i) Expert Advisors to assist the Inquiry in identifying, obtaining, interpreting and evaluating the evidence within their particular area of expertise, currently: (a) Paediatrician; (b) Paediatric Anaesthetist; (c) Nurse in Paediatric Intensive Care; and (d) National Health Service Hospital Management
    (ii) Experts appointed to 'peer review' the work of the Expert Advisers, currently: (a) Internal Medicine/Nephrology; (b) Paediatric Anaesthetist; and (c) Paediatric Intensive and Critical Care Nursing
    (iii) Experts on a case by case basis as Expert Witnesses
    (iv) Experts to provide commissioned 'Background Papers'

13. You have been identified as an expert whose role falls within category (iii) above. You are asked to consider Protocol No. 4 from this perspective.

Background to Adam

14. Adam Strain was born with cystic, dysplastic kidneys with associated problems with the drainage of his kidneys related to obstruction and vesico-ureteric reflux. He was referred to the Royal from the Ulster Hospital in Dundonald and came under the care of Dr. Maurice Savage (Consultant Paediatric Nephrologist)[1] and Mr. Stephen Brown (Consultant Paediatric Surgeon).

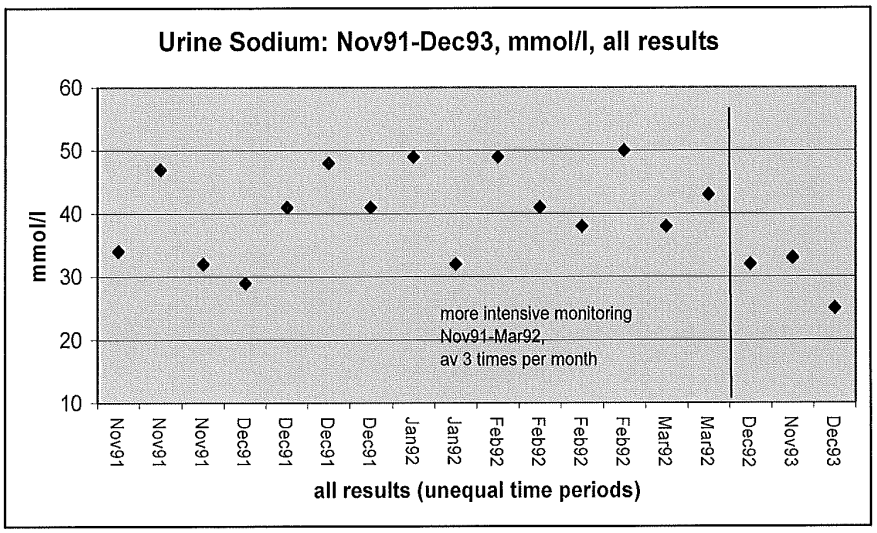
15. Adam had multiple operations to his urinary tract, during which he was largely under the care of Mr. Stephen Brown. He had re-implantation of his ureters on 2 occasions and had nephrostomies performed during the early months of his life. On several occasions, he was critically ill and required care in PICU and a brief period of dialysis due to acute renal failure. In addition a fundoplication procedure was carried out in 1992 when Adam was less than a year old, to help

[1] Now Professor Maurice Savage

prevent gastro-oesophageal reflux. Eventually he required all his nutrition through a gastrostomy tube and, in 1993, he had a cystoscopy and PEG gastrostomy. In October 1995, he had his PEG changed.

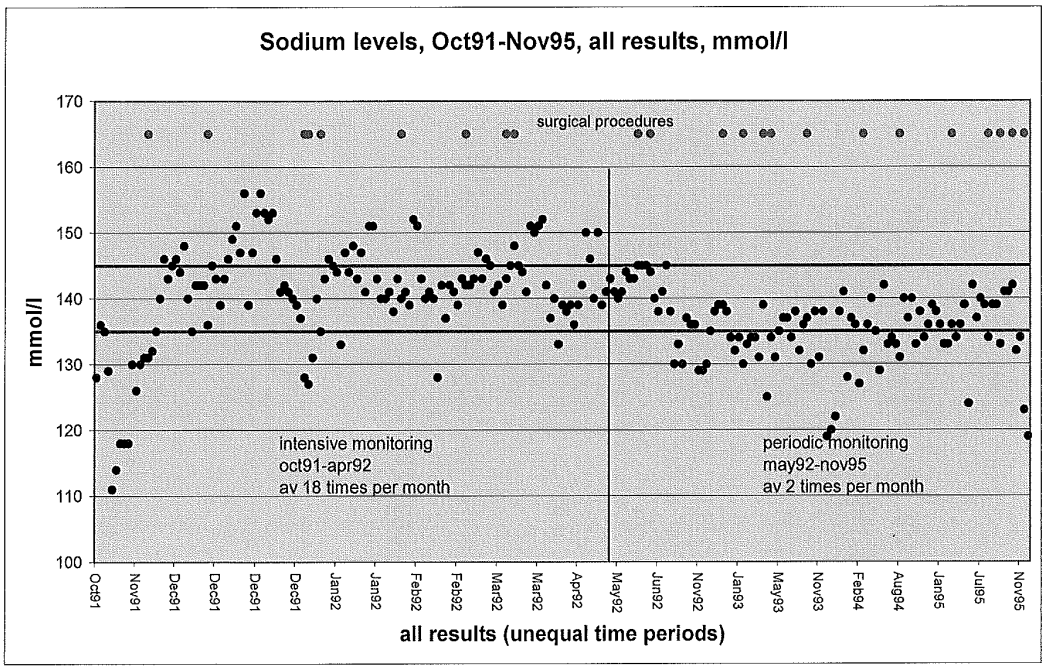
16. Adam was subject to recurrent urinary tract infections and his renal function deteriorated to the point where he required dialysis for uraemia. His mother was trained in the home peritoneal dialysis technique so that he could be dialysed at home. His urine output was quite large but of poor quality and he was described as being polyuric. Biochemistry tests carried out when he was a few months old showed the sodium content of his urine to be 29 - 52 mmol/l.

17. A graph of all Adam's recorded urine sodium results is shown below:



18. According to his nephrologist, Dr. Maurice Savage, Adam had a potential for hyponatraemia and he received sodium supplements in his feeds.

19. A graph of all of his recorded blood sodium levels is shown below with 135-145mmol/l being the normal range:



20. The management of his serum sodium levels appears to have been largely carried out under the care of Messrs. Victor Boston and Stephen Brown, both Consultant Paediatric Surgeons. Despite that, his recorded sodium levels for 1995, the year of his transplant surgery, show one very low result of 124 mmol/l and a number below the normal range of 135-145 mmol/l. Furthermore, in Adam's first year of life his recorded sodium levels fell as low as 111 mmol/l, 114 mmol/l and 118 mmol/l. Thereafter there were numerous occasions when his recorded serum sodium levels fell below the normal range.

21. Adam was put on call for a kidney transplant once he was placed on dialysis. His tube feeds in the months prior to the transplantation surgery were slightly over 2 litres per day and he passed in excess of 1 litre of urine each day.

22. Adam received the offer of a reasonably matched kidney on 26th November 1995. The donor kidney had been removed from a heart-beating 16-year-old donor with normal renal function at 1.42am on 26th 1995. Transplant surgery was scheduled for 6.00am on 27th November 1995.

23. At 23:00 on 26th November 1995, Adam's serum sodium was recorded as 139 mmol/l and Hb 10.5 gm/dl. As part of the preparation for his surgery, his feeds were changed although there remains an issue as to exactly what they were changed to. According to his charts, he was given 952 ml of 'clear fluid' to stop 2 hours before going into theatre. The nursing records do not state the nature of the 'clear fluids' given. Some witnesses have claimed that fluid was Dioralyte (containing 60 mmol of sodium chloride/L). However, Dr. Maurice Savage corrected his Deposition to delete 'Dioralyte' and substitute 'N/S Saline Dextrose'. In any event, it is thought that he received just over 1 litre of fluids.

Apparently it was planned between Dr. Maurice Savage and Dr. Robert Taylor (Consultant Paediatric Anaesthetist) that Adam should receive intravenous fluid (75 ml/h) after the tube feeds were discontinued and have his blood chemistry checked before going to theatre. Those checks did not take place. Once again, there are different views as to why they did not. On one basis, it was because it proved difficult to achieve venous access, whilst on another it was because of the potential delay in receiving results back from the laboratory.

24. The main events surrounding Adam's pre-operative, peri-operative and post-operative care and treatment are summarised in the following table:

Date	Event	
26.11.95	20:00	Adam brought to RBHSC
	22:00	Evaluation Nursing Report taken by SN Murphy
	23:00	i.v. fluids commenced prescribed by Dr. Larkin (Community SHO); Results of investigations recorded by Dr. O'Neill (SHO) as haemoglobin 10.5g/dl, sodium 139mmol/l and urea 16.8 mmol/l; Dioralyte instead of Nutrison gastrostomy feeds on Dr. Taylor's (Consultant Paediatric Anaesthetist) advice
	23:30	Medical history and clinical examination taken by Dr. O'Neill (Senior House Officer): (i) temp. 36.4; (ii) pulse 97; (iii) blood pressure 108/56; (iv) weight 20.2kg
27.11.95	01:30	SN Murphy recorded i.v. fluids tissued and informed Dr. O'Neill
	05:00	i.v. cannula reinserted (although this is recorded, it seems that the cannula was not actually reinserted) Between 23:00 and 0500 952ml of 'Dioralyte' given internally. Peritoneal Dialysis cycles as normal (750 ml fluid volume 1.36% Dextrose solution – 8 cycles given before theatre). Dialysis stopped at approximately 05:00
	06:55	Adam arrival in theatre. Anaesthesia induced.
	07:00	Dextrose saline fluids (0.18% NaCl in 4%glucose) started i.v. by Dr. Taylor – 500 ml given up to 07:30. Epidural inserted by Dr Montague. Arterial line inserted by Dr Taylor.
	08:00	Central Venous Line inserted via right subclavian vein initial reading of 17 mmHg (considered by Dr. Taylor to be unreliable due to incorrect position of the CVP catheter tip. Transplant surgery started by Mr. Keane (Consultant Urologist); further 500 ml of Dextrose saline fluids given up to 08:45
	08:30	Donor kidney removed from ice; 400 ml HPPF given
	08:45	Rate of Dextrose saline fluids slowed (500 ml given up to 1100) and 500 ml Hartmann's solution commenced
	09.15	400 colloid fluids (HPPF) given
	09:32	Results of pH Blood Gases and Electrolytes received, showing sodium at 123 mmol/l ('normal' shown on the report as 135-145) and haematocrit at 18% (Adam's normal being 30%3) and haemoglobin 6.1g; 250 ml packed red blood cells given
	10:45	200 ml colloid fluids (HPPF) and 250 ml packed red blood cells given
	11:00	Skin closure by Mr. Brown (Mr. Keane having apparently left due to an emergency); neostigmine and glycopyrolate administered by Dr. Taylor to reverse the neuromuscular blockade; blood loss recorded from swabs (328 ml), suction (500 ml) and other (300 ml)

Date	Event	
	circa 11:55	Adam failed to wake, did not breathe and pupils fixed and dilated
	12:05	Adam transferred to PICU for ventilation of his lungs and assessment; puffy appearance with central venous pressure (CVP) approx. 30 mm Hg dropping to 11 mmHg; Mannitol 50 ml prescribed and reduction in fluids
	12:15	Adam's appearance bloated
	19:35	First brain stem test carried out by Dr. Webb (Consultant Paediatric Neurologist)
28.11.95	09:10	Second brain stem test carried out by Dr. Webb (Consultant Paediatric Neurologist)
	circa 11:30	Ventilatory support withdrawn and lines removed
29.11.95	14:40	Autopsy commenced by Dr. Alison Armour (Senior Registrar Forensic Medicine, State Pathologist's Department) at the Mortuary for the Royal Group of Hospitals
22.12.95		Histological slides sent to Professor Jeremy Berry (Professor of Paediatric Pathology, University of Bristol) for a second opinion
12.01.96		Brain was cut after fixation. The brain, spinal cord and histological slides were seen by Dr. Meenaskshi Mirakhur (Consultant Neuropathologist, Royal Group of Hospitals)

25. A post-mortem was carried out on 29th November 1995 by Dr. Armour who reported the cause of Adam's death as: 1(a) cerebral oedema due to (b) dilutional hyponatraemia and impaired cerebral perfusion during renal transplant.

26. For the purposes of her Report, Dr. Armour sought a second opinion on the histological slides from Professor Jeremy Berry (Professor of Paediatric Pathology). He was sent slides of: (i) the native kidneys and the donor kidney; (ii) spleen; (iii) lungs; (iv) liver; (v) lymphnode. He noted that there was unexplained cellular change in the hepatocytes scattered throughout his liver but he did not know the significance of it. He concluded that the transplanted kidney was infracted (dead) at or before the time of transplantation.[2]

27. Dr. Armour also sought a second opinion on the brain and related material from Dr. Meenaskshi Mirakhur (Consultant Neuriopathologist) and sent her the brain, spinal cord and histological slides. Blocks were taken from: (i) right frontal white matter; (ii) left cingulated gyrus; (iii) left basal ganglia; (iv) right and left hippocampus; (v) left occipital lobe; (vi) cerebellum; (vii) pons in toto; (viii) thalamus and the brain was photographed sequentially. Blocks were also taken from: (i) cervical; (ii) thoracic; (iii) lumbar. Apparently Dr. Mirakhur's views were consistent with Dr. Armour's description of and comments on the brain in her Report on Autopsy[3]

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2 Ref: 011-007-020 (Report) – attached; Ref: 011-029-151 (letter of instruction) - attached

3 Ref: 011-010-034 - attached

28. The Report on Autopsy records the fluids given to Adam. Dr. Armour also reports and comments that the fixed weight of the brain at post-mortem was 1,680gms, the average weight for a boy of this age being 1,300gms and the average weight of a man's brain being 1,450gms and that it was the *"effects of this massive swelling of the brain which caused his death"*.[4]

29. The Inquest that was subsequently conducted into Adam's death on 18th and 21st June 1996 recorded the Verdict that the cause of his death was:

> 1(A) Cerebral Oedema
> due to
> (B) Dilutional Hyponatraemia and impaired cerebral perfusion during renal transplant operation for chronic renal failure (congenital obstructive uropathy)
>
> Findings:
> The onset of cerebral oedema was caused by the acute onset of hyponatraemia from the excess administration of fluids containing only very small amounts of sodium and this was exacerbated by blood loss and possibly the overnight dialysis and the obstruction of the venous drainage to the head

30. The Coroner, Mr. John Leckey, was assisted in reaching that Verdict by Dr. Edward Sumner (Consultant Paediatric Anaesthetist) who was retained to prepare a Report on the circumstances of Adam's death. Dr. Sumner concluded in his Report dated 22nd January 1996:

> I believe that on a balance of probabilities **Adam's gross cerebral oedema was caused by the acute onset of hyponatraemia** (see reference) from the excess administration of fluids containing only very small amounts of sodium (dextrose-saline and plasma). This state was exacerbated by the blood loss and possibly by the overnight dialysis.
>
> A further exacerbating cause may have been the obstruction to the venous drainage of the head. If drugs such as antibiotics were administered through a venous line in a partially obstructed neck vein then it is possible that they could cause some cerebral damage as well.
>
> (Emphasis added)

31. Dr. Sumner also gave evidence at Adam's Inquest and his Deposition of 18th June 1996 records him as having expressed the following views:

> All the fluids given after dialysis may have been given to increase central venous pressure. It may have had the effect of causing the dilution of the sodium in the body. **Fluid balance in paediatrics is a more controversial area with a variety of views. With kidney transplants one gives more fluids than in other operations** *["it is usual to be generous with fluids to maintain a CVP of 10-12 to optimise perfusion of the new kidney and to establish its urine-producing function"*[5]*]*. When the new kidney is perfused it is vital that sufficient fluids are available. I got the impression that Dr. Taylor was not believing the CVP readings he was getting. I believe they were probably correct but high. I think I would have believed them. A high CVP can

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4 Ref: 011-010-040 - attached

5 See Dr. Sumner's Report of 22nd January 1996 at ref:011-011-059 – attached

> mean too much fluid has been administered[6] ... The **low sodium was indicative of the hyponatraemia. Below 128 is a hyponatraemic state**.
>
> (Emphasis and parenthesis added)

32. Dr. Robert Taylor (Consultant Paediatric Anaesthetist) gave evidence at the Inquest. His Deposition of 21st June 1996 shows that he disagreed with Dr. Sumner's principal finding:

> **I cannot understand why a fluid regime employed successfully with Adam previously**, led on this occasion to dilutional hyponatraemia ... I believe that **the underlying cause of the cerebral oedema was hyponatraemia (not dilutional)** during renal transplant operation.
> ...
> Adam was the only child with polyuric renal failure I have anaesthetised for renal transplant. He needed a greater amount of fluid because of the nature of the operation *["All the more important in this case is the need to avoid dehydration that will deprive the donor kidney of sufficient fluid to produce urine"[7]]*. I believe the fluids given were neither restrictive or excessive. **The new kidney did not work leading to a re-assessment of the fluids given**. This made us think we have underestimated fluid and we gave a fluid bolus at 9.32.
>
> (Emphasis added)

33. The circumstances of the calculation of the fluids given to Adam and the actual amounts involved (bearing in mind his 'polyuric condition'[8]) are important issues for the Inquiry as they go to whether Adam's hyponatraemia might have been avoided by appropriate fluid management.

Requirements

34. The Inquiry team requires your assistance with the following matters, arising out of the material received to date and the guidance of the Inquiry's Expert Advisors:

    (1) Given Adam's age and his weight of 20.2kg, is 1,302gm or 1,320gm a reasonable figure for the pre-operative (dry) weight of Adam's brain? What is the possible range of Adam's pre-operative dry brain weight?

    (2) What effect (if any) does the process of 'fixation' have on brain weight?

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6 Dr. Sumner prepared his Report on the basis that Adam received 900mls of Dioralyte. See at ref: 011-011-055 - attached. That figure was corrected in correspondence between the Coroner and Dr. Armour but it is not clear that the correspondence from Adam's mother referring to the lower figure was passed to Dr. Sumner. Dr. Armour thought that the difference between the two figures made no difference to her opinion on the cause of Adam's death: *"It is not just the volume of fluid he received but the type."* See at ref: 011-079-214 - attached

7 See Deposition at ref:011-014-100 - attached

8 See letter dated 2nd March 1995 from Mr. Maurice Savage (Consultant Paediatric Nephrologist) to Dr. Scott (Adam's GP) explaining: *"The problem is he still needs about 2 litres a day because of his polyuric renal failure"* (Ref: 057-072-133) - attached.

(3) What is your experience or knowledge of a child of 4 years and weighing 20.2kg having a post-mortem fixed brain weight of 1,680gm?

(4) What (if any) is the significance of the weight of Adam's cerebellum having been recorded at 154gm and his brain stem at 22gm?

(5) Dr. Armour weighed Adam's brain on 29th November 1995 (therefore pre-fixation) and appears to record in her notes a weight of 1,302gm corrected to 1,320g. She also records in her description of organs after fixation that Adam's fixed brain weight was 1,680gm. What is the likely reason for the difference between the pre-fixation and fixed brain weights?

(6) In your experience how likely is it that a post-mortem fixed brain weight is inaccurate, ie what are the likely chances of 1,680gm, which is recorded in the Report of Autopsy as the fixed weight of Adam's brain at post-mortem being inaccurate due to uncalibrated scales or human error?

(7) What extra-cerebral fluid space is available in a 4 year old like Adam to allow 'reserve capacity' to accommodate cerebral oedema?

(8) If Adam had any degree of cerebral oedema before surgery, what effect is that oedema likely to have on such a 'reserve capacity'

(9) If Adam's total body water was expanded by 10 per cent at 09:32 on 27th November 1995, what effect would that have had on his brain weight?

(10) Is it possible to calculate what proportion of cerebral oedema can be accounted for by the volume of fluid given and the rapid fall in serum sodium?

(11) If Adam had suffered irrecoverable brain damage from oedema by some time between 09:32 and 11:30, is any continuing accumulation of oedema relevant?

(12) Is it possible to calculate how much oedema there was likely to have been at 09:00 and 11:30? If so, how could that be done? Is it possible to estimate what Adam's brain might have weighed at 09:32 (when his serum sodium was recorded at 123mmol/L) and at 11:30 (when his serum sodium was recorded at 119mmol/L)? If so what is your estimate of his brain weight at both of those times?

(13) Describe and explain, to the best of your expertise, the likely progression or otherwise of cerebral oedema in a child who is being kept alive only by mechanical means. In particular:

(a) state if it was likely that Adam's cerebral oedema would have progressed further after 11.55 on 27th November 1995 when he was reported as failing to awaken from anaesthesia and having fixed dilated pupils

(b) if so, how long and to what extent the cerebral oedema would have progressed thereafter. In particular, whether it would have progressed until ventilation was abandoned 22 hours later

(c) explain how relevant it was to his death given that timing of death depended not on a clinical event but on an artificial construct, namely the performance of brain stem death tests at 12 hourly intervals

(14) What effect (if any) could any impairment to Adam's cerebral blood flow whilst he was in the operating theatre have had to the level of his cerebral oedema when he left there? If it could have had an effect on it, then what contribution (if any) could that have made to his ultimate gross cerebral oedema, assuming that he was adequately oxygenated in PICU?

(15) State whether you believe there is any suggestion or possibility of Adam having cerebral tissue hypoxia, separate from anything caused by dilutional hyponatraemia itself:

(a) If so, state whether it is possible that such hypoxia would have been sufficient to cause or materially contribute to the cerebral oedema which developed

(b) Explain the role, if any, of anaemia in the pathogenesis of cerebral hypoxia and/or cerebral oedema

(16) If Adam was anaemic at some stage (until correction by transfusion), then what effect (if any) could that have had on his cerebral oedema?

(17) Can the use of dopamine contribute to cerebral oedema? If so, how and to what extent? Given the amount of dopamine prescribed for Adam and when it was administered to him, is it possible that it could have affected the extent of his cerebral oedema? If so, can you estimate the likely extent of its contribution in Adam's case?

(18) Does the weight of Adam's brain at 1,680gm imply a cause of death other than dilutional hyponatraemia? If so, what might that be? What is the likely contribution to that brain weight of:

- The dilutional hyponatraemia
- Any cerebral tissue hypoxia between operation and death

- Any anaemia Adam suffered during surgery and
- The dopamine that was administered

(19) The likely effect on the weight and appearance of Adam's brain of all that occurred between his coning in the operating theatre and the withdrawal of ventilatory support, including the process of coning itself as well as the fluids and medication administered to him over that period

35. To assist you we have attached an index of 'key documents' together with a file of the documents that would appear to be of especial significance. Please request any other documents that you consider relevant for the preparation of your Report

Conclusion

36. It is of fundamental importance that the Inquiry receives a clear reasoned opinion on these issues.

37. Your assistance on the Inquiry's requirements should be provided in the form of a fully referenced Expert's Report.

INDEX OF KEY ACCOMPANYING DOCUMENTS

Tab.1 Brief

Tab.2 Selected Inquest Documents:

Depositions:
- Dr. Maurice Savage (Ref: 011-015-109)
- Dr. Alison Armour (Ref: 011-010-030)
- Dr. John Alexander (Ref: 011-012-079)
- Dr. Robert Taylor (Ref: 011-014-096)

Reports:
- Professor Peter Berry (Ref: 011-007-20)
- Dr. Edward Sumner (Ref: 011-011-042)

Tab.3 Selected PSNI Documents:

Reports:
- Professor Peter Berry (Ref: 093-030)
- Professor Risdon (Ref: 093-031)
- Medical opinion of Dr. Edward Sumner, including PSNI brief (Ref: 094-001-001 and Ref: 094-002-002)

Tab.4 Selected Inquiry Documents:

Initial Witness Statements of:
- Ms. Debra Slavin (1st)
- Dr. Maurice Savage (1st & 2nd)
- Mr. Patrick Keane (1st, 2nd & 3rd)
- Dr. Robert Taylor (1st & 2nd)
- Dr. Mary O'Connor (1st, 2nd & 3rd)
- Dr. Edward Sumner (1st)

Other Inquiry documents:
- Letter dated 2nd March 1995 from Dr. Maurice Savage to Adam's GP, Dr. Scott (Ref: 057-072-133)
- Autopsy Request Form
- Letter dated 10th May 2011 from State Pathologist's Office to the Inquiry attaching the contemporaneous notes of Dr. Alison Armour
- Adam's medical notes and records for 26th November 1995 - 29th November 1995