

SUMMARY OF EVENTS

Re: Adam's cause of death and the role of Hyponatraemia

Inquiry Experts

1. The Inquiry engaged the following Experts to address generally the role of the Nephrologists, Anaesthetists, Surgeons and Nurses involved in Adam's case:
 - (i) Dr. Malcolm Coulthard (Honorary Consultant Paediatric Nephrologist, Royal Victoria Infirmary, Newcastle upon Tyne) whose Reports concern issues such as the roles and responsibilities of the Nephrologists involved in Adam's case (Dr. Savage and Dr. O'Connor), an explanation as to Adam's renal function, as well as expert analysis of the management of Adam's fluid balance and electrolytes
 - (ii) Dr. Simon Haynes (Consultant in Paediatric Anaesthesia and Intensive Care - Freeman Hospital, Newcastle upon Tyne) whose Reports address matters such as the role and responsibilities of the Anaesthetists involved in Adam's case (Dr. Taylor and Dr. Montague), the relationship between Surgeons and Anaesthetists in the operating theatre during transplant surgery, as well as providing analysis of Adam's fluid balance
 - (iii) Mr. John Forsythe (Consultant Transplant Surgeon, Royal Victoria Infirmary, and Honorary Professor of Surgery, University of Edinburgh) and Mr. Keith Rigg (Consultant Transplant Surgeon, Nottingham University Hospitals NHS Trust) who have provided joint Reports on amongst other matters the role and responsibilities of the Surgeons involved in Adam's case (Mr. Keane and Mr. Brown), the skills required and involved in a paediatric renal transplant including the techniques used for anastomoses, as well as the relationship between the Surgeons and Anaesthetists during transplant surgery
 - (iv) Ms. Sally Ramsay (Independent Children's Nursing Advisor) has provided a Report on the nursing aspects of Adam's care

2. In addition the Inquiry engaged Experts to provide Reports on a number of specific issues, including:
- (i) Professor Peter Gross M.D (Professor of Medicine and Nephrology) who has provided Reports on hyponatraemia and an analysis of Adam's fluid management
 - (ii) Professor Fenella Kirkham MB, BChir FRCPCH (Professor of Paediatric Neurology, Institute of Child Health, London and Consultant Paediatric Neurologist, Southampton General Hospital) who was asked by the Inquiry to give a neurological opinion into the effect of the infusion of fluids during surgery had on Adam's brain and the possible contribution, if any, of venous obstruction to Adam's cerebral oedema. Professor Kirkham has since queried the exact role that dilutional hyponatraemia played in Adam's death, and has suggested cerebral venous thrombosis and PRES as alternatives. This issue was discussed at length by the Inquiry's Experts in their meetings on 22nd February 2012 and 9th March 2012.
 - (iii) Dr. Caren Landes (Consultant Paediatric Radiologist) who has examined and reported on chest x-rays taken of Adam at 13:20 on 27th November 1995 and 21:30 on 27th November 1995¹
 - (iv) Dr. Waney Squier (Consultant Neuropathologist and clinical Lecturer, John Radcliffe Hospital, Oxford) who provided an expert Neuropathological opinion from histological slides that she made from the tissue blocks of Adam's brain. She also examined a sequence of photographs of Adam's brain taken at autopsy by the pathologist Dr. Alison Armour and received input from Dr. Philip Anslow on a post-surgical CT scan of Adam's brain
 - (v) Dr. Philip Anslow (Consultant Neuroradiologist, Radcliffe Infirmary, Oxford) who was brought in by Dr. Squier to assist in interpreting CT scans taken of Adam's brain on 7th July 1995² and the post-surgical scan taken at approximately 13:15 on 27th November 1995³

Emerging differences amongst the Experts

¹ Ref: 207-005-010

² Ref: 057-114-332

³ Ref: 058-038-182

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3. Clear differences emerged between the Inquiry's Experts and Adam's clinicians as to his cause of death and the role played by dilutional hyponatraemia. It was also clear from the reports of the Inquiry's Experts that there were differences amongst them on those issues.
4. However, until the preliminary Report provided by Professor Kirkham on 16th February 2011⁴ (Tab 1a) the shared view of the Inquiry's Experts was that dilutional hyponatraemia was the major cause of the acute cerebral oedema that led to Adam's death. That is not to say that there were not some differences amongst them, principally these concerned the role of a possible ligation of Adam's left internal jugular vein as described in Dr. Armour's Report on Autopsy⁵ and its contribution to any obstruction to the venous drainage from the head as referred to in Dr. Sumner's Report of 22nd January 1996⁶ and his evidence on 18th June 1996.⁷
5. The Report of Professor Kirkham signalled a change to there being a common view on dilutional hyponatraemia amongst the Inquiry's Experts. She introduced in her preliminary Report the explanation that: *"on the balance of probabilities, chronic venous sinus thrombosis was a likely cause of Adam's previous rather subtle neurological problems"* and that it was likely that: *"further acute thrombosis in the venous sinuses was associated with acute posterior cerebral oedema during the operation"*.⁸ She also expressed the view that the: *"development of PRES [posterior reversible encephalopathy syndrome, for which Adam had at least 3 risk factors (anaemia, blood transfusion, immunosuppression) contributed to the rapid development of mainly posterior cerebral oedema"*.⁹
6. Professor Kirkham then does go on to deal at paragraph 54 of her preliminary Report with dilutional hyponatraemia. She summarises and addresses in turn the bases of the argument that: *"Adam's acute cerebral oedema and brain death was caused by dilutional hyponatraemia"*.¹⁰ She concludes with: *"Although it is possible that the compensatory mechanisms were overwhelmed because of the rapidity of the fall in sodium and the associated shift of water into the brain along an osmotic gradient, on the balance of probabilities the rapid development of fatal posterior cerebral oedema was secondary to acute on chronic cerebral venous thrombosis, probably with the*

⁴ Ref: 208-002-017

⁵ Ref: 011-010-034

⁶ Ref: 011-011-063

⁷ Ref: 011-011-049

⁸ Ref: 208-002-035

⁹ Ref: 208-002-037

¹⁰ Ref: 208-002-038

additional development of posterior cerebral oedema similar to that seen in cases of PRES".¹¹

7. Following Professor Kirkham's preliminary Report, the Inquiry's clinical Experts had two lengthy meetings, one on 22nd February 2012 (Tab 8) and one on 9th March 2012 (Tab 9). Both meetings were recorded and there is a transcript for each one.¹² Professor Kirkham's preliminary Report and those two meetings then generated a considerable number of Reports from the Experts as they explored and challenged their differences and the bases for them:

(i) Dr. Anslow:

- Note of 16th February 2012¹³ dealing with certain queries raised by Professor Kirkham, prior to the completion of her preliminary Report (Tab 2)

(ii) Dr. Coulthard:

- Report of 15th March 2012¹⁴ on CVP presenting his arguments as to an error in zeroing (Tab 3a)
- Report of 15th March 2012¹⁵ dealing with the two papers cited by Professor Kirkham in her preliminary Report, namely: (a) Paut et al: 'Severe hyponatraemic encephalopathy after paediatric surgery: report of seven cases and recommendations for management and prevention'; and (b) Sicot & Laxenaire: 'Death of a child due to posttonsillectomy hyponatraemic encephalopathy', together with a third paper (Tab 3b)
- Report of 16th March 2012¹⁶ on free water balances, which corrected his Report on the same subject earlier that day and includes 2 pages of calculations based on Dr. Taylor's statement of 1st February 2012. This report corrects an error in a report dated 16th February 2012, also enclosed for completeness. (Tab 3c)
- Report of 16th March 2012¹⁷ providing responses to queries raised during the Experts' meeting on 9th March 2012 and Dr.

¹¹ Ref: 208-002-039

¹² Ref: 307-007-073 & 307-008-162

¹³ Ref: 208-004-051

¹⁴ Ref: 200-019-226

¹⁵ Ref: 200-018-222

¹⁶ Ref: 200-021-254

¹⁷ Ref: 200-020-232

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Taylor's statement of 1st February 2012,¹⁸ as well as recalculating his own table, 'Adam's perioperative fluid balance',¹⁹ and those originally produced by Dr. Haynes,²⁰ Professor Gross²¹ and Dr. Taylor²² (Tab 3d)

- Report of 17th March 2012²³ providing his final views from the perspective of a paediatric nephrologist (Tab 3e)

(iii) Professor Gross:

- Report of 18th March 2012 on the Experts' meeting of 22nd February 2012²⁴ (Tab 4a)

(iv) Dr. Haynes:

- Report of 20th February 2012 responding to the Report of Professor Kirkham dated 16th February 2012²⁵ (Tab 5a)
- Supplementary Report of 6th March 2012²⁶(Tab 5b)
- Report of 18th March 2012²⁷ on his final position having regard to the Expert Reports to date and the two meetings of Experts (Tab 5c)
- Summary Report of 18th March 2012²⁸ (Tab 5d)

(v) Dr. Squier:

- Report of 17th February 2012 responding to Professor Kirkham's Report of 16th February 2012²⁹ (Tab 6a)
- Report of 15th March 2012³⁰ on her final position. (Tab 6b)

8. Subsequently the following additional Reports were received from the Inquiry's Experts:

(i) Professor Gross:

¹⁸ Ref: WS-008-6, p.1

¹⁹ Ref: 300-062-119

²⁰ Ref: 300-063-122

²¹ Ref: 201-008-203

²² Ref: 300-061-117

²³ Ref: 200-022-260

²⁴ Ref: 201-015-215

²⁵ Ref: 204-008-353

²⁶ Ref: 204-009-361

²⁷ Ref: 204-012-378

²⁸ Ref: 204-013-389

²⁹ Ref: 206-006-113

³⁰ Ref: 206-010-120

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- Report of 23rd March 2012 on the Experts' meeting of 9th March 2012³¹ (Tab 4b)
- (ii) Professor Kirkham
- Final report of 28th March 2012³² (Tab 1b)
9. The debate amongst the Inquiry's Experts deals with complex medical issues, some of which may well be being developed out of research that is still ongoing.
10. Although even that is not accepted by all of the Inquiry's Experts. On the one hand Dr. Coulthard states at page 3 of his Report of 20th February 2012 that he does not consider that there is anything new in PRES but that it is simply a radiological description for acute hypertensive encephalopathy, which is something that all Nephrologists know they need to manage.³³ Whilst on the other hand Dr. Haynes acknowledges at paragraph 25 of his Report,³⁴ also of 20th February 2012, that PRES is increasingly recognised as an entity and believes he has come across some cases. He also agrees in that Report that PRES can be considered where there is no obvious underlying cause for the cerebral oedema, albeit that in Adam's case there was such a cause, namely the dilutional hyponatraemia.³⁵
11. As a pathologist, Dr. Squier approached the issue of PRES from a different perspective. She explains in her Report of 22nd February 2012 that PRES is not yet a condition diagnosed pathologically³⁶ and Dr. Anslow states in his Note of 18th February 2012 responding to certain queries raised by Professor Kirkham that: "*PRES is a diagnosis best made on MRI*".³⁷ However, Dr. Squier nonetheless comments at paragraph 50 on PRES as being "*a very interesting condition that was well worth consideration*".³⁸

³¹ Ref: 201-016-284

³² Ref: 208-007-068

³³ Ref: 200-014-207

³⁴ Ref: 204-008-353

³⁵ Ref: 204-008-353

³⁶ Ref: 206-006-114

³⁷ Ref: 208-004-051

³⁸ Ref: 206-006-114

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The ongoing research and study on the matters being considered and debated by the Inquiry's Experts is well illustrated by the published literature they cite in their Reports.

Cause of Adam's Cerebral Oedema and Death

12. The cause of Adam's death is recorded on the Verdict on Inquest³⁹ as:

"I(A) Cerebral Oedema

Due to

(B) Dilutional hyponatraemia and impaired cerebral perfusion during renal transplant operation for chronic renal failure (congenital obstructive uropathy)"

The findings made by the Coroner were that:

"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"

13. The Inquiry has had to consider the cause of Adam's cerebral oedema and death, including:

- (i) The role of dilutional hyponatraemia, if any
- (ii) Any other causes or contributing factors including:
 - Chronic cerebral venous sinus thrombosis
 - Acute cerebral venous sinus thrombosis
 - Thrombosis of the paravertebral plexus
 - Reduced jugular venous drainage or possible venous obstruction
 - Cerebral blood flow, anaemia and reduced cerebral O₂ delivery/low CO₂
 - Posterior Reversible Encephalopathy Syndrome (PRES) during surgery
 - Hypoxia
 - Seizure(s) during surgery
 - Halothane in anaesthetic
 - Pre-existing central nervous system condition

³⁹ Ref: 011-016-114

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14. To assist, the Legal Team produced two Schedules – 'Summary of Key Point: Pre-Experts' Meetings'⁴⁰ (Tab 7a) and 'Summary of Key Points: Post-Experts' Meetings'⁴¹ (Tab 7b) – that set out in summary form the positions of each of the Inquiry's key experts on the issues (Professor Kirkham and Professor Gross and Dr. Squier, Dr. Haynes and Dr. Coulthard) before the their Expert Meetings on 22nd February 2012 and 9th March 2012 and after those meetings.
15. The 'key points' included in the Schedules are:
 - (i) Adam's development
 - (ii) The medical literature
 - (iii) The risk factors for chronic / acute venous thrombosis
 - (iv) Venous sinus thrombosis
 - (v) The effect of reduced jugular venous drainage
 - (vi) PRES
 - (vii) Adam's presentation during surgery
 - (viii) Arguments on brain death caused by dilutional hyponatraemia

Next steps

16. In the light of the continuing differences between the Inquiry's Experts a second opinion was sought from you. Your Report has been received and considered.
17. We now attach Reports from the Inquiry's other Experts, including the Reports of Professor Kirkham, and ask that you consider whether they alter in any way the opinions that you have expressed in your Report. If they do not, then a brief note confirming that will suffice. However, if you do wish to revise you opinions as a result of those Reports then we ask that you provide a Supplemental Report drawing attention to anything further and your reasoning. Any such Supplemental Report should be

⁴⁰ Ref: 306-016-130

⁴¹ Ref: 306-017-146

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referenced and we ask that you provide a copy of any new material on which you rely.