Summary Report on Adam Strain to the Inquiry Into Hyponatraemia Related Deaths:

This report represents my final comments on events relating to the death of Adam Strain. It draws on previous reports made to the Inquiry by myself and follows reflection of the comments made both by myself in these previous reports and by others – namely Dr Malcolm Coulthard, Professor Fenella Kirkham, Professor Peter Gross, Dr Waney Squier, and members of the Inquiry team led by Ms Monye Anyadike-Daynes QC.

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18th March 2012

Signed: Simon R-Haynes 18th March 2012

Dr Simon R. Haynes, 18th March 2012

1: My qualifications:

MBChB University of Edinburgh 1983
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My expertise:
I have been employed as a consultant in paediatric cardiothoracic anaesthesia and intensive care at the Freeman Hospital in Newcastle upon Tyne, England, from August 1994 – present. My clinical duties are centred around the provision of anaesthesia and intensive care to children with congenital heart disease undergoing cardiothoracic surgery or invasive cardiological investigation as well as some other general paediatric anaesthetic duties. My specialist interest is the management (including mechanical cardiac support) of life-threatening cardiac failure and cardiopulmonary transplantation in children.

In the course of this work I care for seriously ill children both in the operating theatre and in the intensive care unit. Management of fluid balance, electrolyte abnormality, acute renal impairment, blood loss, brain injury in the critically ill child, central venous access, and management of immunosuppression are some components of my routine work particularly relevant to the Inquiry with regard to Adam Strain.

I am a full time NHS consultant. I have no formal academic duties. I am an author on 31 peer reviewed papers.

I was Clinical Director of Cardiothoracic Surgery and Anaesthesia at the Freeman Hospital from 2000 -2006; this is an administrative role which among other things included overseeing the clinical governance activity of a directorate of 30 consultants and ensuring that the infrastructure for the clinical work of the directorate is fit for purpose. The role is carried out in addition to full-time clinical duties.

1. Clinical Summary of Adam Strain:

Adam was born on 4th August 1991. He had dysplastic kidneys and obstructive uropathy requiring many subsequent surgical interventions. He had significant renal impairment which progressed to renal failure, ultimately needing long term peritoneal dialysis which was carried out at home by his mother with assistance and input as required from the paediatric nephrology dept at the Royal Belfast Hospital for Sick Children. He continued to produce urine, but his kidneys could not regulate the quantity or quality of the urine produced, meaning that particular attention was required to his fluid and electrolyte intake. He was placed on the kidney transplant waiting list, and was admitted to RBHSC on the evening of 26th November 1995 for a kidney transplant which was carried out the following day (27th November). At the end of the transplant operation he did not breathe and his pupils were fixed and dilated. He was artificially ventilated. He was declared brain stem dead in accordance with UK guidelines on 28th November 1995 and ventilatory support was withdrawn shortly after.

2. Specific aspects of Adam's care and related matters

The expected outcome of renal transplantation in children in 1995;

It would have been an extremely rare event for a child to die during the course of a renal transplant operation. One large published series contemporary to Adam's transplant did not describe any operative deaths in 321 children transplanted (204-002-082 – 85), and all of a further 62 patients from Northern Ireland transplanted after Adam's death are noted by Dr O'Connor to have survived renal transplant surgery (WS 14/2/ 21-22). Many children like Adam having renal transplantation would have had numerous previous surgical interventions. Blood loss requiring transfusion would be common during the course of the operation (204-002-073)

The arrangements for paediatric renal transplantation in Belfast:

As far as I can ascertain, surgeons whose main are of practice was adult urology carried out paediatric kidney transplantation at RBHSC, where responsibility for subsequent care was maintained by the paediatric nephrology team. A small number of paediatric renal transplants were carried out. The implication of this is that either the experience would be diluted among a large number of clinicians, or the service was dependant on a small number of individuals in whom the experience was concentrated. This is discussed in greater length in my previous report (204-002-038).

The operating theatre infrastructure and staffing arrangements in RBHSC at the time of Adam's transplant

I have discussed this in detail in previous reports (204-002-026 – 028, 204-002-096 – 097, 204-004-145 – 147, 204-004-179 – 188). It is noted by Professor Gross in his email to the Inquiry dated 6th February 2012 that Dr Taylor would have been busy at the start of the anaesthetic for Adam's transplant with a variety of tasks. That is undoubtedly the case; it is my opinion that Dr Taylor placed himself under time pressure by starting at 0700h rather than 0600h, and it concerns me greatly that there was no nominated anaesthetic assistant (nurse or ODP) to assist Dr Taylor at the start of Adam's anaesthetic. My conclusion is that the standard of anaesthetic assistance offered to Dr Taylor at the start of Adam's anaesthetic was poor, and was not in keeping with that expected throughout the UK and subsequently recommended by both the Association of Anaesthetists of Great Britain and Ireland and the Royal College of Anaesthetists. It is my opinion therefore that failure of RBHSC to ensure that Dr Taylor had adequate, appropriately trained non-medical assistance may well have prevented him from performing his duties to the best of his abilities whilst anaesthetising Adam.

Although not supplied with a specific inventory of equipment available it is my impression that the RBHSC was suitably equipped for carrying out renal transplantation in children

The experience and training of Dr Taylor, who anaesthetised Adam for his transplant operation

I understand that this was the first paediatric renal transplant that Dr Taylor had undertaken with overall responsibility. He had some training in solid organ transplantation at Toronto Sick Children's Hospital from ~~1998-90~~ 1988 – 90 and had been a consultant at RBHSC from 1991 onwards, during which time he undoubtedly would have gained a great deal of experience in the management of a wide variety of conditions in very ill children of all ages, Therefore this is not an issue. My opinion remains as previously iterated (204-002-021 – 22, 204-004-147) namely that Dr Taylor did have the necessary experience, training and competence to safely anaesthetise Adam for his transplant.

The anaesthetic given by Dr Taylor

The anaesthetic *per se* was in my opinion appropriate for Adam's renal transplant. Intravenous access was secured, epidural analgesia utilised, endotracheal intubation and ventilation was appropriate, there was no episode of hypoxaemia noted nor was there any hypotension. Appropriate anaesthetic agents were used. Central venous access was sought and an arterial line was put in place.

However there were two significant failures on Dr Taylor's part. Firstly he did not take the opportunity the evening before the transplant to visit Adam and his mother. Secondly, he did not gain a clear understanding of Adam's clinical condition – with especial reference to his renal function, fluid and electrolyte balance and to the history of central venous cannulation. A more ordered discussion with Dr Savage could have better appraised him of Adam's fluid and electrolyte needs. Equally, it is my opinion that Dr Savage might have been more forceful in his discussions with Dr Taylor regarding Adam's fluid management.

Adam's fluid balance and the intravenous fluid therapy administered by Dr Taylor during the course of his transplant operation.

This has been the subject of extensive analysis and discussion by the various experts reporting to the Inquiry. It is my firm belief that Adam received an excessive volume of hypotonic fluid (0.18% saline in 4% glucose) early during the course of his anaesthetic. It is also my firm belief that this resulted in dilutional hyponatraemia with subsequent cerebral oedema.

Dr Taylor's assessment of Adam's fluid requirement during the operation was incorrect – Adam received an excess volume of intravenous fluids; but the crucial error made by Dr Taylor was not the volume of fluid given but the type of fluid given; he gave Adam 1500 mls of hypotonic fluid early during the anaesthetic, equivalent to 1200 mls of electrolyte-free water and 300 mls of isotonic saline. When the published literature is searched for the effects of this, three French publications come to light. Dr Coulthard in his report dated 15/3/2012 examines the three published case reports of Paut, Auroy and Sicot and notes that Adam was administered a similar amount of free water as children described by these clinicians but over a much shorter period of time – hence Adam's serum sodium concentration would have decreased at a much greater rate.

Dr Taylor notes on the anaesthetic chart that Adam's intraoperative maintainence requirements for fluid were 200 ml/h. That would be the volume of fluid he thought was required to be given to replace urinary losses, evaporative losses from the operation site, and insensible losses. All other fluid given should have either been isotonic or blood. Thus, Dr Taylor should only have needed (by his calculations) to have given 900 mls of 0.18% saline/4% glucose during the operation from 0700 - 1130. He gave 1500 mls, early on in the operation. My calculations as previously noted by the Inquiry were that Adam would have needed 72 mls/h (14 ml/h insensible losses throughout, 4ml/kg/h evaporative loss from the operation site during the actual operation, and 58 ml/h urine) = 602 mls – which I would have given as Hartmann's solution, but in 1995 many anaesthetists would have given this as a hypotonic fluid. I would describe my calcultion as erring on the high side – I assume that Adam produced urine throughout, which may not have been the case.

Dr Taylor's intention was that Adam should have had a blood sample taken for electrolyte assay prior to transfer to the operating theatre. This was not done. That being the case, Dr Taylor should at the very least have carried out point of care testing using the blood gas analyser as soon as he had secure vascular access following induction of anaesthesia, and at regular intervals thereafter – I would suggest that hourly would have been appropriate. When he eventually did this at around 0930h, and a sodium concentration of 123 mmol/l was obtained, he should have acted upon it (as previously stated 204-002-033 – 4) to correct it.

Debate has occurred with regard to the accuracy of electrolyte assay using blood gas machines. The manufacturer has been contacted by the Inquiry, and is firm in the belief that the machine available, if used correctly, is accurate. (WS 180/1 p4) Even if less accurate than formal laboratory assay, an abnormally low measurement should have prompted Dr Taylor to take corrective action.

No steps were taken to monitor Adam's urine output during the operation although urine output was measured after the operation. It would have been preferable to have had an indwelling urinary catheter inserted. If there was a real reason from the anatomical/surgical viewpoint not to insert a urinary catheter, then this decision should have been commented upon in the notes. Other centres catheterise children at the start of a renal transplant operation (204-002-067, 200-004-084). If the patient being transplanted was known to have anuric renal failure, than there would be less doubt about the intraoperative fluid balance, and bladder catheterisation at the start of the operation would be less important. If Adam did indeed only produce 49 mls of urine during the operation rather than the 58 mls/h I allowed in my fluid balance calculation, then the fluid balance calculations would be inaccurate by approximately 220 mls. Ie the calculated fluid excess would be 220 mls greater.

Adam's preoperative condition

There has been extensive discussion about Adam's preoperative condition following Professor Kirkham's report. Adam was gastrostomy fed and it was thought that he might have some difficulties chewing and swallowing. Professor Kirkham suggested that this might have represented pre-existing neurological impairment. I have considered both this view and the contrary view expressed by Dr Coulthard that all children with chronic renal failure have feeding difficulties which then resolve following a successful kidney transplant. On balance I acknowledge Dr Coulthard's large experience in caring for children such as Adam and I do not accept that there is anything to suggest that Adam had a pre-existing neurological condition.

Adam was mildly anaemic and had been treated with erythropoietin. I do not believe that this put him at risk. As noted elsewhere, renal

transplantation carries a minimal intraoperative mortality risk, and most, if not all, children having a kidney transplant are either anaemic, on erythropoietin, or both.

Professor Kirkham also raised the question as to whether Adam had previously had a cerebral venous sinus thrombosis. There was no evidence of this at autopsy, nor could Dr Squier support the diagnosis. Although Adam did have the risk of becoming more dehydrated than a child with normal renal function in the presence of any intercurrent illness because of his native kidneys inability to regulate fluid balance, there is nothing to suggest to me that cerebral venous sinus thrombosis had been present in Adam. Severe dehydration is a risk for cerebral venous sinus thrombosis.

Cerebral venous drainage and CVP measurement

This has been discussed at length by the Inquiry. Numerous central venous lines had been placed in Adam, some at a very early age. It is my opinion as previously stated that this almost certainly means that there was some narrowing of the great veins draining his head and neck. it would therefore have been sensible to have arranged for ultrasound examination of these vessels when Adam was placed on the transplant waiting list, and a plan made for gaining central venous access at the time of transplantation depending on the findings. As detailed in my reply clarifying points raised by the Inquiry team following the meeting on 9th March 2012, I am absolutely certain that the CVP reading obtained during Adam's transplant operation could not be relied on either as an absolute number or as a trend monitor.

There is a question as to whether Adam's left facial vein or left internal jugular vein had been tied off in relation to a previous central venous line insertion. I do not think that this question will ever be answered conclusively. Regardless, I do believe it likely, purely because of the number of venous lines inserted during his life that Adam had some vulnerability of the venous drainage of his brain – which might have only become significant once cerebral oedema consequent to hyponatraemia had begun to develop. I do not believe that obstruction to venous drainage of the brain was the primary event initiating the cerebral oedema.

The fact that Dr Taylor took several attempts to insert a central venous line is not an issue in itself. It is my opinion that it might have been prudent, once difficulty was identified with placement, to have inserted the line into a femoral vein, on the opposite side to where the transplanted kidney was to be anastamosed, or to have considered a surgical cut down procedure to cannulate a central vein in the neck.

Dr Taylor correctly identified that the line he inserted was inadvertently directed towards the brain rather than the heart, and that a high value for the CVP had been recorded. It is my opinion that he must have noticed

that the line was advanced a long distance through the skin puncture overlying the right subclavian vein; had he withdrawn it a short distance, a more realistic waveform and pressure reading might have been obtained

Possible risk factors for brain injury in Adam, and discussion of factors which might not have initiated brain injury but which might have have exacerbated the effects of an insult to Adam's brain.

Hyper or hypo capnoea (too much or too little carbon dioxide in the arterial blood). Capnography was utilised by Dr Taylor as part of Adam's anaesthetic monitoring. All the readings obtained are acceptable. Cerebral blood flow is very sensitive to the partial pressure of carbon dioxide in arterial blood (PaCO2). It a patient is over-ventilated and the PaCO2 decreases below normal limits, cerebral blood flow is decreased, potentially compromising the brain. If the PaCO2 is allowed to rise too large a level, cerebral vasodilatation occurs, and if intracranial pressure is already increased for another reason, then intracranial pressure may rise critically, also compromising the brain.

Abnormal cerebral venous drainage has been discussed in the section above

Halothane was the volatile anaesthetic agent used. It causes cerebral arterial vasodilation which alone would not have caused any problem, but again, if intracranial pressure was increasing as cerebral oedema developed, then cerebral arterial vasodilation caused by halothane might have precipitated a critical increase in intracranial pressure. I emphasis again that in 1995 halothane was widely used, especially in paediatric practice

Head down position. I have discussed this at some length in my response to queries raised following the meeting of 9th March 2012. It is likely that Adam would have been positioned slightly head down during the transplant to make pelvic structures more accessible to the surgeon. As stated in my previous comment, head down positioning will cause an increase in intracranial pressure and result in a decrease in cerebral perfusion pressure.

Anaemia:
At 0932h the sample analysed by the blood gas machine showed that Adam had a haematocrit of 18%, equivalent to a haemoglobin concentration of 6.1g/dl. Although there had undoubtedly been some blood loss by this time, I am certain that the majority of this degree of anaemia was dilutional, caused by the administration of an excessive volume of intravenous fluid, as demonstrated by my calculation in my response to queries raised following the meting on 9th March 2012.

Although this is a very low haemoglobin concentration, I do not accept that it is low enough to have caused brain injury – given that there was nothing

to suggest that Adam's cardiac output was low or that the blood pressure was low at that point in time. Had there been another compromising factor such as a low blood pressure, or if cerebral perfusion had already become compromised by cerebral oedema causing increased intracranial pressure, then it would have been significant.

Posterior Reversible Encephalopathy Syndrome (PRES).

An alternative diagnosis of Posterior Reversible Encephlopathy Syndrome (PRES) has been suggeted by Professor Kirkham. Anaemia, steroids and ciclosporin are said to be associated with this syndrome. Methyl prednisolone was not given to Adam until hyponatraemia was established, and ciclosporine was not given until return to the paediatric intensive care unit. I have looked after children who have had seizures following heart transplantation who have shown brain changes on imaging, the presentation has always been several days postoperatively, usually in the presence of high ciclosporin blood levels, minor electrolyte abnormalities, and poorly controlled hypertension. It is my opinion that PRES cannot be considered as a diagnosis in Adam.

A summary of the most important medical literature with regard to the administration of hypotonic fluids and hyponatraemia

1. Holliday MA, Segar WE. Pediatrics 1957:19:823-832. The Maintenance need for water in parenteral fluid therapy

Maintenance intravenous fluid replacement requirements for children have historically been provided using hypotonic fluids. The need to replace fluid losses (eg stomach contents, exceptional intestinal losses, losses into the extracellular compartment etc) with 0.9% saline has also been recognised. The recommendation for hypotonic fluid as maintainence fluid stems from this publication by Holliday and Segar in 1957. This publication has been held in high regard over the years and is often quoted, frequently outwith the original context and in situations different from those intended by the authors; its entire focus is the relationship of water requirements for children as based on their energy expenditure, not taking into consideration other factors which may be present in the postoperative state.. It *does not* address ways of achieving the normality of electrolyte concentrations in blood required to maintain cellular integrity and function during the postoperative period These authors comment on the fact that both human breast milk and cow's milk have a sodium concentration of approximately 30 mmol/litre (similar to that found in 0.18% Saline/4% glucose). Concern at the time was that children's kidneys would not be able to excrete adequate amounts of sodium if fluid replacement was with 0.9% saline solution (sodium concentration 154 mmol/l). Following this recommendation, it became standard practice to provide maintainence

intravenous fluid in children with a solution such as 0.18% saline in 5% glucose.

2. Arieff AI. New England Journal of Medicine 1986:314;1529-1535. Hyponatremia, convulsions, respiratory arrest, and permanent brain damage after elective surgery in healthy women.

Arieff in 1986 drew attention to the dangers of hyponatremia during the postoperative period. He described major neurological events with catastrophic consequences which occurred in 15 previously well women ocuring over a 10 year period. They were all significantly hyponatraemic, and had all received significant volumes of hypotonic intravenous fluids. Although not describing hyponatraemia in children, this paper identifies women as being particularly at risk of hyponatraemia during the postoperative period.

3. Arieff AI, Ayus JC. British Medical Journal 1992: 304; 1218 – 1222. Hyponatraemia and death or permanent brain damage in healthy children.

This paper is much cited, and in conjunction with the subsequent publication of work from Professor Bohn's group in Toronto Children's Hospital (see Halberthal below), it has really highlighted the need for the medical community to be aware of the dangers of hyponatraemia caused by the administration of hypotonic fluids to children during the immediate postoperative period. Sixteen previously healthy children aredescribed who either died or received permanent brain damage because of postoperative hyponatraemia. These occurred among 24412 consecutive surgical admissions in one North American Hospital.

4. Halberthal M, Halperin ML, Bohn D. British Medical Journal 2001:322; 780 – 782. Lesson of the week: acute hyponatraemia in children admitted to hospital: retrospecttive analysis of factors contributing to its development and resolution.

Comment and discussion of the mechanism by which acute hyponatraemia (defined as serum sodium measured as 130 mmol/l or less within 48 hours of admission) developed in 23 children admitted to Toronto Children's Hospital, thirteen during the postoperative period. Of the 23 children studied, 5 died and a sixth sustained brain damage. Clear recommendations are made as to how best to prevent this happening.

The mechanisms why hyponatraemia can develop are listed further on in the report. There are two simple messages in this paper: firstly, the administration of hypotonic fluids to children with a variety of illnesses carries the risk of causing hyponatraemia, and secondly, if intravenous

fluids are administered, it is important to measure the serum sodium concentration, and act upon any abnormality identified.

5. Moritz ML Ayus JC. Pediatric Nephrology 2005: 20; 1687-1700. Preventing neurological complications from dysnatremias in children.

Previous literature is reviewed, and a strong recommendation is made for 0.9% saline to be routinely used as maintainence fluid in children; the authors argue that it is safe, and that this will prevent life-threatening hyponatraemia

6. NHS National Patient Safety Association, Patient safety alert 22, 2007
Following review of the information available including the above literature a patient safety alert was prepared and distributed throughout the UK in 2007. The dangers of hyponatraemia in association with intravenous fluids in children are highlighted.

There are many other papers on the subject, and all promote the same message. It is clear that there was much discussion in the medical literature about hyponatraemia in children from the mid 1980's onwards. During this time no single doctor or institution would have encountered serious problems from hyponatraemia more than sporadically. From a personal point of view I certainly became increasingly aware during the latter part of the 1990's, as did my colleagues, of the dangers of hypotonic intravenous fluids. With hindsight it is regrettable that Holliday and Segar's 1957 work has become so widely embraced within medical teaching and textbooks that there is still resistance to the use of isotonic fluids in children today, and that lack of awareness of the dangers of hyponatraemia persists in many quarters.

Clinical governance at RBHSC following Adam's death:

I have not been provided with documentation regarding minutes of departmental mortality meetings and any subsequent actions taken at RBHSC by senior clinicians or management to ensure that a similar catastrophe did not occur again.

I find it disappointing that it has taken Dr Taylor over 16 years to accept that he made some errors whilst he was responsible for the care of Adam Strain

3. My opinion regarding the cause of Adam's death

It is my opinion that Adam Strain died as a consequence of cerebral oedema caused by a rapid decrease in serum sodium concentration at the time of kidney transplantation. The decrease in serum sodium concentration was caused by the administration of a large volume of hypotonic intravenous fluid over a short period of time.

Once established, the effects of the cerebral oedema may have been exacerbated by some or all the following: impaired cerebral venous drainage, head down positioning, dilutional anaemia, and cerebral vasodilatation caused by halothane.

I cannot say with certainty when brain stem death occurred. The failure to breathe once neuromusciular blockade had been reversed at the end of the operation and the failure of the pupils to react to light at this time are some of the signs of brain stem death.

Dr Simon R. Haynes: 18th March 2012.