This is a report by

Dr Malcolm Coulthard

requested by the *Inquiry into Hyponatraemia-Related Deaths*

in response to the document, "Queries – M Coulthard – 26-10-11"

11/11/2011

Format I will respond in order to the document "Queries – M Coulthard – 26-10-11

QUERIES FOR EXPERT NEPHROLOGIST:
DR. MALCOLM COULTHARD
ADAM STRAIN

(a) You state at page 27 of your first Report to the Inquiry, dated 4th August 2010, that because of the effect of the peritoneal dialysis, *"there is a huge safety margin which buffers the impact of variations in fluid status that would otherwise result in children becoming either dehydrated or fluid overloaded."* In addition, peritoneal dialysis *"tends to correct any imbalances that may exist in the plasma sodium"*.

Please find attached Adam's dialysis diary completed by his mother in the months prior to his death. An analysis of Adam's fluid loss produced by overnight peritoneal dialysis on 70 nights in July to October 1995 showed variation from about 138 ml to 642 ml; average 290 ml. On one occasion when only 7 cycles were used, loss was reduced to 82 ml.

(i) State whether, given your comment that *"there is a huge safety margin which buffers the impact of variations in fluid status that would otherwise result in children becoming either dehydrated or fluid overloaded,"* it is possible to be in fluid deficit after overnight dialysis.

(ii) State whether the shorter dialysis time than was normal for Adam, i.e. 8 cycles rather than his usual 15 cycles (Ref: 093-006-017), could have had any effect on the ability of his peritoneal dialysis to:

(1) *"buffer the impact of variations in fluid status that would otherwise result in children becoming either dehydrated or fluid overloaded."*
(2) *"correct any imbalances that may exist in the plasma sodium"*.

(iii) In particular, when Adam's dialysis finished at 06:00, state:

(1) Whether you consider Adam was in fluid deficit at that time, and if so, to what degree he was likely to have been in fluid deficit
(2) What you consider his serum sodium concentration was likely to have been at that time.

Response to sections (a)(i) and (a)(ii)

A) FLUID VOLUME

Principles of varied UF requirements

Healthy children can cope with hugely wide variations in their fluid intake by altering how much water they excrete each day as urine. Children with end-stage kidney failure cannot vary the amount of urine that they produce in response to physiological need; they either do not produce any urine, or produce a similar fixed volume each day, regardless of how much they drink. This means that dialysis, which augments and effectively replaces the function of the kidneys, must be flexible in the amount of fluid it removes each day, otherwise variations in how much children drink will lead to either dehydration (if the dialysis takes off too much fluid) or fluid overload (which leads to high blood pressure amongst other things) if it takes off too little.

To prevent symptomatic variations in children's fluid volumes it is necessary to try to regulate their fluid intakes. This may be relatively simple in younger children who are mainly given modified milk feeds, often via a feeding tube and pump, but even then, there will be some days when the child vomits, or hot days when they lose more fluid by evaporation. As children grow older, their fluid intake is much more difficult for their parents to regulate, as they may increasingly demand or help themselves to drinks. Different foods also contain very different amounts of water (compare eating a jelly with eating a chocolate pudding!). The approach of fluid intake regulation is therefore seldom sufficient, and regular adjustments are needed to the amount of water removed by dialysis.

With haemodialysis, this problem is solved by the nurses weighing the child before commencing a dialysis session, and setting the machine to remove a corresponding amount of water to bring the weight down to the non-overloaded or 'dry' weight.

With peritoneal dialysis (PD), although it is possible to alter the overall power of fluid removal by using dialysis fluid with higher osmolality values (usually achieved by an increasing concentration of glucose), the ultrafiltrate (UF) still varies very widely even if the same dose of dialysis (the fill volume and osmolality of the dialysis fluid, and the cycle sequence) is used. It is clinically obvious that this happens in response to the child's fluid removal needs. This makes this form of dialysis much more feasible than it would otherwise be. It is not clear what the mechanism of this effect is, but it is likely that it involves physical forces at the level of the peritoneal membrane, similar to the classic physiological Starling effect across capillary walls.

The result of this is that if children start their overnight PD 'drier' than usual, less UF is obtained, and conversely more UF is achieved after an increased intake. We have noted during hot summer spells that all of our patients' UF values consistently fall, which we attribute to them losing more fluid from perspiration than usual. To test if this common effect was seen in Adam, I have looked at the data recently provided to me for him, in the form of his mother's diaries.

Adam's mother's diary

Adam's mother maintained a diary during the time that she carried PD out on him at home in which she noted down the date, the total UF volume (as well as its component volumes of the initial drain, the recorded UF for the cycles, and the final manual drain), his weight going on to dialysis and his weight coming off, as well as some extra comments on occasions. She did not record every piece of information each time, and did not record every night, apparently.

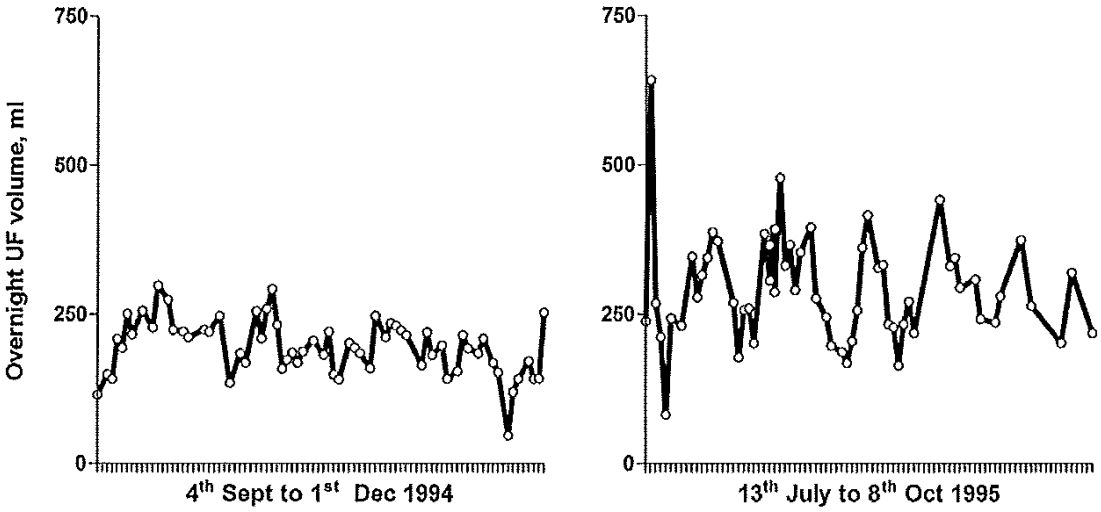
Weights

Unfortunately, Adam was always weighed at home on a scale which only measured to the nearest 0.5 kg, so the weight losses overnight are insufficiently sensitive to allow us to compare the recorded UF values with their corresponding overnight weight changes.

However, it is clear from reviewing the weights coming off dialysis in the mornings, even despite the imprecision of weighing only to the nearest 0.5 kg, that he came off at consistently similar weights each day, with the main changes in weight being the gradual upward trend due to growth. Our own experience of large numbers of parents routinely recording and graphing their children's weights going

on and coming off PD at home, but using scales accurate to 0.1 kg, is that this pattern of a relatively stable morning weight superimposed on a gradually increasing weight is almost universal.

Overnight UF values
It is clear that Adam's UF values do vary quite widely from day to day, despite him consistently coming off dialysis apparently well in the mornings. This can be seen in the figure below in which the UF values for Adam are graphed for two 3-month periods. On the left is the autumn of 1994 when Adam was new to PD and weighed about 15 kg, and on the right is nearly a year later when his weight was around 19 to 20 kg, not long before his transplant.



In each panel, there is an obvious middle range which the UF values fall within, but with some outliers. The range of the plots spans 47 ml to 642 ml. It would be helpful in understanding this if we could correlate these outlier days with the clinical events, but for the most part this is not possible to do 16 years later. However, there is data in the clinical notes that relates to the 2 extreme values for the right-hand panel.

On Friday 14/07/1995 the UF was especially high at 642 ml. In the case records for that day [058-033-120], it is recorded that Adam was admitted to the ward as a day case for a planned blood transfusion. He received a unit of whole, white-cell poor, tissue-typed blood as his haemoglobin had fallen to just 5.7 g/dl. That is, he was administered approximately 500 ml of blood, and this was followed by a greater than usual UF volume.

On Monday 17/07/1995, just 3 days later, the UF was especially low at 82 ml. In the case records for that day [058-033-121], it notes that he had been spiking temperatures to 39.5℃ over the weekend, and that he was admitted to the ward for investigations. The timings are not recorded, but the tests he had were extensive, including a scintigraphy scan, and it is noted that he was generally unwell. It is at least likely that he would have had less to drink than usual on a busy clinical investigation day whilst unwell with fever. His weight coming off, at 19 kg, was the median (typical) for that time.

It is clear from Adam's mother's diary that the UF value of 82 on that day was genuine, and not a machine error or transcription error. She notes that the machine only completed 7 cycles that night, and that it registered slow fill and drain periods to the cycle. This is what happens if the UF falls considerably below the expected range for that individual child. The expected values are entered into the PD machine's computer, and if much less than the anticipated drain volume is delivered (because the child is not ultrafiltering as normal, for instance), then the machine waits longer for this to happen. This means that the cycle time is automatically extended, and at the end of the programme time a smaller number of cycles will have been completed.

Unfortunately, I cannot find a clinical note corresponding to his low UF of 47 in November 1994, but such variations are commonly seen after relatively unremarkable events, such as the feed pump not working properly overnight, or the child vomiting.

Conclusion from diaries
Although these diaries do not provide direct proof that Adam's UF tended to vary responsively to his fluid status, as is commonly observed in other children, they provided a strong suggestion that this was the case for him too.

This therefore supports my previous statement that alterations in Adam's dialysis and fluid routine is far less likely to produce a volume imbalance in him than would be the case if PD simply removed fluid in an automatic regular and consistent way, as haemodialysis does, instead of responding to the physiological circumstances.

In any case, in the morning of 27/11/95 when he was not receiving his PD, he was also not receiving his usual fluid intake. This means that one effect would have tended to balance the other, and his overall fluid balance was unlikely to have been significantly perturbed by the events in the few hours prior to his transplant.

Is it possible for PD to cause dehydration?
One characteristic of PD as compared to haemodialysis is that the UF rate is unpredictable, and cannot be precisely controlled. Although the UF does tend to follow the child's physiological needs, it does not do that in an absolute or consistently reliable way. However, this tends to be in the direction of it not removing a sufficient volume. Older children in particular who tend to drink more than their advised fluid volume frequently become gradually more and more overloaded over a period of time, and in our experience, they then often need a brief admission to be dialysed more aggressively, both for longer and with a higher osmolality fluid.

It is definitely possible to induce a state of fluid depletion using aggressive dialysis with high concentration fluids. I have personally seen this happen in a tragic way in hospital with a 3.5 kg baby who was being dialysed overnight with insufficient monitoring, using the strongest strength dialysis fluid, rendering the child shocked and permanently damaged. I have never seen fluid depletion caused by the standard nearly isosmolar fluids that Adam was routinely dialysed with. I am not aware of reports from others of this either.

B) PLASMA SODIUM

Principles of sodium movement
During PD, sodium moves across the peritoneal membrane between the plasma in the blood vessels supplying the abdominal organs and the dialysis fluid by 2 mechanisms, convection and diffusion.

Convection This is the movement of sodium and other dissolved chemicals with water as it travels across the peritoneal membrane in response to osmolar changes and the Starling forces that produce ultrafiltration. As the water moves, it drags the chemicals with it. This means that when Adam ultrafilters water into his peritoneal space, it will contain sodium at a concentration very similar to that in plasma. In other words, as the water is lost, it has no impact on the sodium concentration of the plasma left behind in his body.

Diffusion This is the movement of chemicals across a semi-permeable membrane, down their concentration gradient. Put simply, if the fluid in the peritoneum was much lower in sodium than that the plasma was, then the sodium ions would tend to drift from the blood into the peritoneal space, and the concentration in the blood would fall. Similarly, if the sodium concentration in the dialysis fluid was made much higher than in the blood plasma, the ions would move into the blood and increase its concentration.

PD fluid is made with a sodium concentration in the normal physiological range. This means that if the blood starts off with a normal sodium concentration, there will be no net movement in or out of the body as the ions shift both ways at equal rates, and no overall diffusion will occur. It also means that if the blood starts off with a normal sodium concentration, but this tends to be gently diluted by the child being fed with milk, or any other fluid with a lower salt level than blood, or by the administration of a hypotonic intravenous fluid, then the shift of sodium from the PD fluid into the blood by diffusion will keep the plasma concentration from falling too far. In other words, the more abnormally low the plasma sodium falls, the more sodium moves into the plasma to buffer the fall, thereby keeping it more-or-less normal at all times.

The limiting factor in this mechanism is the relatively low efficiency of PD, certainly compared to haemodialysis. However, in small children PD is at its most efficient, and as a result of this, significant perturbations of the post-dialysis plasma sodium levels are rare. The reason why PD is more proportionately more efficient in smaller individuals compared to larger ones is because of their relative dosing and membrane sizes.

Dialysis fluid is instilled at cycle volumes of approximately 40 ml/kg, usually with an upper limit of 2.5 litres in adults, so a 70 kg adult would receive a slightly lower dose of 36 ml/kg. In adults, for practical and cost reasons, typically 4 to 6 cycles are administered per day or overnight, while small children are given many more, in Adam's case a routine of 15 cycles. Finally, the surface area of the peritoneal membrane, which is the dialysis membrane in PD, varies not with the patient's weight, but with their body surface area. Because the weight of a body varies with its length cubed, while its surface area varies with the length squared, it is obvious that the surface area to weight ratio varies with length. Put into human terms, this means that the relative size of the PD membrane is twice as great in a child of half the height of an adult. Combing these factors, a 20 kg child will have at least twice the dialysis efficiency as an adult. This may be a factor in the very effective way in which PD limits perturbations in the plasma sodium in small children, compared to adults.

Response to sections (a)(iii)

In a previous report for this inquiry, I completed a fluid balance table for Adam. In that, I concluded that he was likely to have been in approximately normal balance at the time that he arrived in the operating theatre to be anaesthetised for his transplant. I have attached a copy of that form to this report as Appendix 1, for convenience.

A more detailed reply would be that I assessed that his **water** balance was between 8 and 308 ml in positive balance. In real terms, this means that he was somewhere between being in precise water balance, and being about 300 ml overloaded. Even allowing for all of the roundings and assumptions that inevitably went into this analysis, it would certainly exclude him having been water deficient.

It also concluded that his **sodium** balance fell by up to 9 mmol between his arrival in hospital and his arrival for his anaesthetic. This is a fall of almost exactly 0.5 mmol/kg. Since the distribution volume of sodium is about 65% of the body weight, this would be likely to have reduced the plasma sodium concentration by approximately 1 mmol/l. This is an amount which is below the laboratory error of repeated sodium estimations, which is about ±3 mmol/l.

In conclusion, I think that Adam arrived in theatre adequately filled with fluid, and with a plasma sodium concentration which was about 1 mmol/l lower than his earlier level (which I know is now not considered to be entirely certain), a fall that was so small that it may not have been detected by routine biochemical analysis. He was therefore in a safe and suitable condition to have an anaesthetic,

and did not require to have extra fluid administered because of 'fluid deficits', and certainly not any hypotonic saline.

(b) Adam was prescribed with 50ml 20% mannitol intravenously by Dr. Mary O'Connor at 12:00 on 27th November 1995 on his transfer to PICU after surgery. He was prescribed a further 100ml of 20% mannitol by Dr. Meenakshi Bhat from 14:00 that day. He passed 115ml of urine between 12:00 and 13:00, 35ml between 13:00 and 14:00, 90ml between 14:00 and 15:00 and thereafter between 80ml and 140ml/hr of urine (a mean of 90ml/hr) between 15:00 and 23:00. Input was approximately 247ml between midday and 23:00. By 20:00, he had produced 809ml of urine. Within 24 hours of arriving in PICU, he had produced 1,460ml of urine. (Ref: 057-018-027)

(i) Please explain your view of the urine output capabilities of Adam's native kidneys having regard to the effect of the mannitol stimulus in PICU.

In my previous reports, I explained that I would not have expected Adam's urine output to increase at all in response to an increase in the fluid intake. This is because by the time a child's kidneys have reached end-stage (that is when they are unable to maintain the child's condition safely without support from either dialysis or transplantation), they have always lost their ability to respond to variations in physiological requirements. Thus, they are simply unable to respond to the body's signals to alter factors such as the sodium or water excretion rates. In effect they are always working 'flat out'. They never meet their physiological targets, and the body's signalling systems are continuously switched fully on, but the kidneys cannot function any quicker. This means that any extra signals, such as the need to excrete yet more water in response to being given extra, makes no difference to the amount of urine they make.

Adam's response to a mannitol infusion post-operatively is entirely consistent with these predictions. Mannitol is a sugar that is not metabolised by the body, other than by being excreted by the kidneys. If it is given to a child with normal kidney function it will be removed by the kidneys, and in the process it will carry water with it by osmotic forces; that is it will cause them to increase their urine production rate. However, if it is given to a child in end-stage kidney failure it will remain in their blood for many days, unless it was dialysed out.

Adam was given 30 grams of mannitol (a total of 150 ml of 20% solution) intravenously, which is a moderately large dose, and definitely sufficient to cause a substantial diuresis in a child whose kidneys are capable of responding to it. Instead, Adam passed a total of 1460 ml of urine over the ensuing 24 hours, the same rate of urine production he was estimated by Dr Savage to have on a normal day.

Note that I have ignored any apparent hour-by-hour variations in the urine excretion rate in his case, even though he had a catheter in situ, which might lead one to assume that his urine was being drained at the same rate as it was being made. However, this cannot be assumed in children with gross vesicoureteric reflux and capacious ureters. In that case, the urine effectively drains into reservoir 'pockets' which themselves drain into the bladder differently according to the position that the child is lying in. As a result, when he is turned on the bed (a regular process carried out to prevent bed-sores in a comatose or otherwise immobile patient), the size of the urine reservoir changes. Thus, a typical child like Adam may appear to stop producing urine for a long period on his right side, only to have a large volume drain when he is turned onto his left or onto his back, or vice versa. This is why the only figure I have considered is the 24 hour value, as this will be least effected by these short-term variations.

(c) Please find attached a table showing the various phases in a paediatric renal transplant operation. Please modify it, as you consider appropriate, so that it

reflects what you consider should have happened and identify under those phases the personnel who you consider should have been involved.

Table attached as Appendix 2.

(d) Please find attached further statements as follows:(You already have copies of these)

(i) Dr. Taylor (WS-008-3 dated 28th September 2011)
(ii) Dr. Taylor (WS-008-4 dated 28th September 2011)

Please provide your comments on the conduct of Dr Taylor in the light of your view as to what could and should have happened. If those statements provoke further amendment or comment to your previous reports, please outline any such amendments or comments.

In my view Dr Taylor made some fundamental errors when he anaesthetised Adam for his transplant. I have referred to some of these previously in my Report of 04/08/10 (section H) and my Report of 15/03/11 which was particularly focussed on Dr Taylor's police testimony. Here, I am being asked to consider his responses to further questions posed to him, documents WS-009/2, 3 and 4, dated May and September 2011. I have also been provided with a copy of the second page of a document apparently used to request for a post-mortem examination to be undertaken on Adam, which was apparently written by Dr Taylor, and have been asked to consider the contents of that.

I am aware that this reply risks being repetitious, but my purpose is to consider (a) the overall most key issues, and (b) how Dr Taylor's replies in 2011 compare to his earlier responses.

1) **Dr Taylor's understanding about when to administer 0.18% saline/ glucose solution.**

In his earlier reports, Dr Taylor stated (incorrectly) that an intravenous solution containing glucose and 0.18% sodium chloride (N/5 saline) was equivalent to administering a physiological isotonic solution. In September 2011, he accepts that this is not the case [WS-008/3; page 39 (110)].

He also stated earlier (also incorrectly) that N/5 saline was appropriate to use in expanding the blood volumes of children, citing a reference in the British National Formulary which he claimed recommended it for treating dehydration (though it did not do this). He no longer appears to be arguing this specific point. However, his post-mortem request note makes it clear that in 1995 he felt that this *was* appropriate management, and his 2011 statements indicate that he still holds this view. In the 1995 document he stated both (a) that he had used 1/5th normal saline in 4% glucose to replace his fluid deficit, and (b) that he regarded Adam's case as being bizarre, and its fatal outcome as a surprise. In 2011, when he was asked why he replaced Adam's fluid deficit at the start of the transplant operation by giving 500 ml of N/5 saline within a 30 minute period, he continued to state [WS-008/3; page 28 (79(a))] that "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".

2) **Dr Taylor's estimate that Adam's urine output needed to be balanced by 200 ml of N/5 saline hourly.**

In his estimate of Adam's regular urine losses, which would need replacing like-for-like to prevent dehydration, Dr Taylor has always stated that he had estimated these to be 200 ml hourly of a dilute solution, best matched by N/5 saline.

In relation to the volume, he has previously stated that his estimate was based on what he was told by Dr Savage, elaborating that Dr Savage had informed him that he had estimated his daily urine output to be about 1.5 litres daily, based upon his fluid intake of just over 2 litres and his other fluid losses. In his May 2011 report, Dr Taylor confirms this by quoting that Adam's "urine output is stated in his records as "PU++ ?how much ?1-2 litres" [WS-008/2; page 8 (15(a))]. Previous expert witness statements have noted that to pass 1.5 litres daily would require a mean urine output of 62.5 ml hourly, not 200, and that a child who did pass 200 ml hourly would have a daily urine output of 4.8 litres. In short, it has been pointed out to Dr Taylor prior to late 2011 that simple mathematics indicate that the estimate of 200 ml was a large error.

Despite this, in September 2011, Dr Taylor continues to justify his calculation of a 200 ml hourly fluid replacement requirement on the same basis, and does not appear to have acknowledged that his mathematics was in error [WS-008/3; page 28 (109(a))]. Instead, he repeats that he reached the value of 200 ml/hour "based on his fluid intake and his known large volume of dilute urine". Indeed, he agrees that if he had known that Adam only passed urine at about 50 to 70 ml hourly, then he "would have administered 0.18%NaCl/4%Glucose at this rate."

3) Dr Taylor's belief that Adam's urine output could increase markedly

In earlier reports, Dr Taylor opined that Adam's urine output was dilute, and had no upper limit (one can only assume that he meant that it was very high indeed), and that this made him capable of being able to handle any amount of fluid he was given. He went on to conclude that this feature made it impossible to induce dilutional hyponatraemia in Adam. This has been discussed since and disputed in reports which I presume Dr Taylor has had access to. In particular, the following points have been made ...

a) That anybody could develop hyponatraemia if they are given enough dilute intravenous fluids.

b) That Adam's urine output is indeed limited because it cannot exceed at most ⅔ of his GFR (the amount of fluid his kidneys filter per hour), that is a theoretical maximum of 125 ml/hour (my report of 04/08/10, section D).

c) Children with end-stage renal failure have kidneys that have a relatively fixed hourly urine volume.

Dr Taylor does not accept these arguments in his 2011 evidence. In May 2011, he repeated his assertion [WS-008/2; page 39 (100(b))] that he "could not retain free water and get dilutional hyponatraemia", and in September 2011, he continued to believe that Adam could increase his urine volume in response to a fluid challenge, though he admitted that he was "not certain if his native kidneys could have coped with [2 litres per hour] of fluid."

4) Failure to take a blood sample for sodium at the induction of anaesthesia

There has been much debate about whether it was mandatory, ideal, or necessary at all to measure Adam's plasma sodium concentration at the end of his period of overnight peritoneal dialysis, either prior to or at the time of induction of anaesthesia. My personal position throughout has been that it was not essential on that particular occasion because it could have been predicted to have been normal or nearly normal, and therefore safe, on clinical grounds. However, others have reasoned that it was important, or at least it would have been better done, and I understand their reasoning.

My concern about Dr Taylor's responses to this element of the debate is not that he did not undertake the blood test, but that his arguments for not having taken this sample are not reasonable. They are ...

a) That it would prolong the cold ischaemia time of the kidney.

The length of time that a kidney is outside the body in cold storage after being removed from the donor and before being grafted into the recipient is necessarily hours with cadaveric transplantation (from dead donors). There is a statistical relationship between this period (the cold ischaemia time) and the chances that the kidney will present some difficulties subsequently, mainly in terms of not starting to function straight away. Under 18 hours is ideal, and the shorter the better. Over 48 hours is highly likely to lead to temporary problems. In Adam's case it was between these extremes.

Dr Taylor continues to cite his concern about the already fairly long cold ischaemia time as the reason that he did not take a blood test. In September 2011, he states [WS-008/3; page 38 (108(b))] that "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."

The problem with this assertion is that taking a blood sample takes very little time indeed in the circumstances that Dr Taylor was in. He has estimated it as taking a minute or two, but this is a pessimistic estimate as during the insertion of a central venous line blood is drawn into a syringe anyway to test its patency, and saving this would take only a few seconds. Even if it took 2 minutes, this would only represent an insignificant difference to the cold ischaemia time, at about one-tenth of 1%.

b) That it would take too long to organise, and exceed their capacity to cope

Dr Taylor has argued previously that he and his colleagues were too busy to deal with the processes of filling in a laboratory form, contacting the laboratory staff, and contacting portering staff at the time of inducing anaesthesia. He further said that the theatre could not spare a nurse to deliver the specimen. This is an extreme claim, especially since a sample could have been taken at induction and sent a little later when the main flurry of initial activity had settled.

He continues to employ this argument; "This would have meant absenting a member of the team at a very busy time" [WS-008/2; page 23 (52(a))], despite reassuring us that the theatre was fully staffed with 3 nurses, "One nurse for the anaesthetist, one as the scrub nurse, and a runner."

5) Failure to monitor Adam's urine output during surgery.

I have argued above that a fundamental reason why Adam was administered too much hyponatraemic intravenous fluid is that Dr Taylor falsely believed that he passed 200 ml of dilute urine each hour. Throughout Dr Taylor's reports he claims to have been monitoring Adam's fluid balance status, and using that information to make adjustments to his fluid administration management plans. However, he agrees that Adam was not catheterised during the operation, and one result of this was that the urine output could not be monitored. Given that the postulated high urine output would have been the largest single contribution to Adam's ongoing fluid needs, this was clearly a mistake, leaving Dr Taylor in the dark about what the true balance was. If he had been catheterised, and his urine drained and measured, it would have become rapidly apparent that Adam was not voiding anywhere near 200 ml per hour, and his fluids could have been slowed down accordingly.

Dr Taylor does not take responsibility for deciding to anaesthetise Adam without catheterising him, either in his earlier reports or in 2011. Instead he indicates that the decision whether to catheterise him was one to be made by the surgeons, who he speculates may have required his bladder to be full to aid surgery [WS-008/3; page 2 (1(a))]. This is a spurious argument.

If Dr Taylor had wanted to monitor Adam more safely by catheterising him to record his urine flow, he could have done so. This decision would have been entirely his, regardless of any conflicting

requirements that the surgeons may or may not have had towards the end of the operation. If they really had wanted him not to be catheterised so that he could have a full bladder, saline could have been flushed back into his bladder at that stage in the procedure. The decision not to catheterise him was entirely Dr Taylor's, and his continuing insistence that he had monitored Adam closely and appropriately without cannot be justified.

6) **Failure to respond to the blood-gas analyser reading of a sodium of 123 mmol/l.**

Dr Taylor's refusal to believe Adam's point-of-care intra-operative plasma sodium concentration of 123 mmol/l, or attempt to validate it, was a crucial missed opportunity which may otherwise have prevented his progression to more profound hyponatraemia. Even now, he does not concede that he should have checked a true sodium level at that point, and instead repeats his decision that he had considered measuring one "at the end of the operation." [WS-008/3; page 16 (1(b))].

It is generally accepted that less reliability may be placed upon a plasma sodium measurement made on a point-of-care instrument than on a laboratory assay, and this may have been particularly so in 1995 when the remit of laboratory staff to ensure constant servicing and calibration of such devices may not have been so clearly defined as it is now. However, they are there for a purpose, which is to signal a warning about possible perturbations in the electrolytes. In this sense they are like many other screening tests, prompting the doctor to undertake a fully valid check. A near-patient plasma sodium as drastically low a 123 should have been responded to as a very important warning sign. I would expect a competent anaesthetist to have reacted to it in two ways; to organise an immediate urgent confirmatory laboratory test, and to take immediate reasonable steps to counter a falling plasma sodium while waiting for the results.

Dr Taylor's evidence remains contradictory on this issue, in that he continues to claim both that he disregarded the sodium of 123 as invalid, and that he acted on it. In September 2011 he says that he "did not rely on it at all." [WS-008/3; pages 36-37 (101(b))], and that if he "had been able to rely on [its accuracy, he] would have stopped the 0.18% NaCl/4%Glucose and administered hypertonic saline". At the same time he tells us that "It did lead me to reassessing his fluids and decreasing the rate of the 0.18% NaCl/4%Glucose" [WS-008/3; page 16 (1(a))], elsewhere describing this as "drastically" slowing it.

(e) Please find attached schedule of haematology/biochemistry results from 26th November 1995 to 28th November 1995. As you can see, the Inquiry has just been made aware that a blood specimen was taken on 26th November 1995 for biochemistry and haematology analysis (Ref: INQ-0450-11). The reports of this analysis are dated 27th November 1995. It is therefore assumed that this specimen was taken and analysed at some time between the initial blood results on admission and the start of surgery. The results do not appear in the clinical notes at any point, but were as follows:

Sodium 133
Potassium 4.3
Urea 16.0
Creatinine 676
Calcium 2.46
Phosphate 1.21
Haemoglobin 10.5
Erythocytes 3.47
PCV 0.321
MCV 92.5
MCHC 32.7
MCH 30.3
Leucocytes 9.54
Platelets 336

Please indicate if this report causes any re-evaluation of your previous conclusions, and if so, what re-evaluations are required.

I am not able to find a formal laboratory report in my bundles for the blood sample taken at 23:00 hours on 26/11/95, but only 2 hand written versions of the results, which differ in one respect. On page [058-035-144] is a hand-written entry indicating a sodium concentration of 139 (I think, though this could be read as 134), and on [057-007-008] is another hand-written entry on a results flow sheet which reads 134. I note that the values for the potassium, urea, creatinine, calcium and phosphate concentrations are the same in both entries, suggesting that these two records are likely to be the same results from the same sample.

While it is possible that the hand-written entries were taken separately on the telephone from a laboratory scientist, it is much more likely that only one of them was transcribed in that way, and that the second entry was copied from the first. Although this copying could have taken place in either direction, it is more likely that it was first written into the notes (which are typically immediately available in the clinical area), and then copied onto a flow sheet (which are typically affixed to the wall/ board/ window of the child's cubicle in my experience). Since the 4 on the flow sheet is clearly written, and the 9 (I think) in the notes is more ambiguous, this direction of copying would appear more likely.

The newly discovered biochemistry blood results are different for every test from any other blood values taken during Adam's admission (see table below). It does seem, therefore, that it was genuinely an extra blood sample, and not a more extreme example of a transcription error of the same sample.

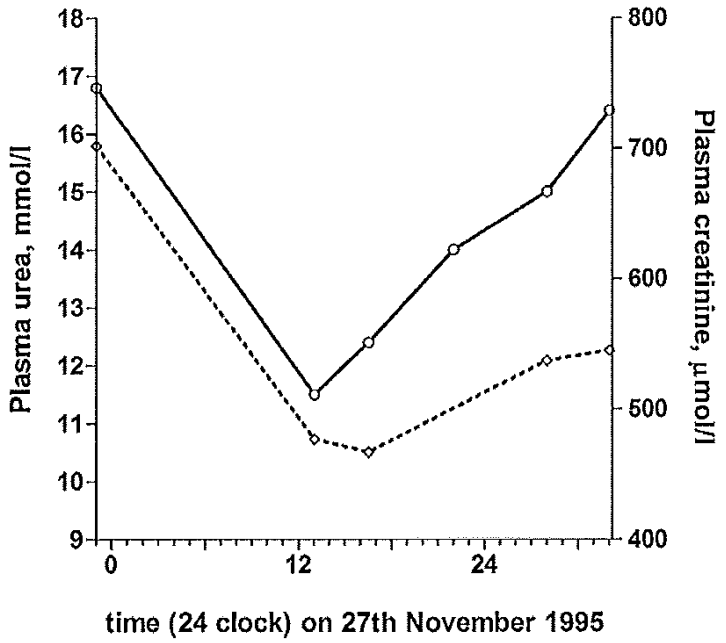
Table of blood results

date	26/11/1995	26/11/1995	26/11/1995	27/11/1995	27/11/1995	27/11/1995	28/11/1995	28/11/1995
time	23:00	23:00	?	13:00	16:30	22:00	04:00	08:00
place	notes	flow-sheet	newly found			flow-sheet		
inquiry ref	[058-035-144]	[057-007-008]	[INQ-0450-11]			[057-007-008]		
sodium	139	134	133	119	124	120	121	125
potassium	3.6	3.6	4.3	4.8	5.0	6.0	6.4	6.3
urea	16.8	16.8	16.0	11.5	12.4	14.0	15.0	16.4
creatinine	702	702	676	477	467		537	545
calcium	2.54	2.54	2.46					
phosphate	1.28	1.28	1.21					

When was it likely to have been taken?
We are told that it was said to have been taken on 26/11/95. If it was taken after the sample from 23:00 hours, then we must assume that it was taken between then and midnight.

The best way to guess at the time it was taken is to compare the urea and creatinine results, as these are removed by dialysis, and then re-accumulate between dialysis sessions. Figure 1 plots these concentrations for the values in the above table, with the urea plotted as open circles and a solid line, and the creatinine plotted as open diamonds and a broken line.

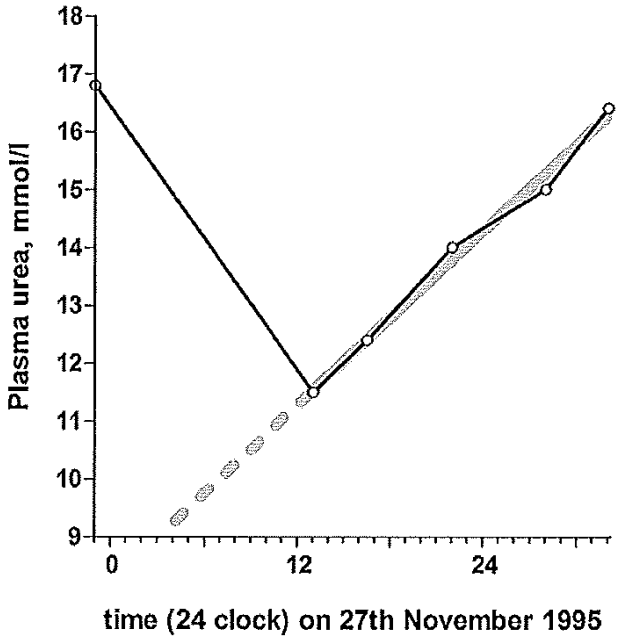
Figure 1 Urea (open circles) and creatinine (open diamonds) concentrations



It is obvious that both of these substances were reduced by dialysis, and were rising thereafter. However, it is also clear that, since dialysis stopped at approximately 6 am, these would have reached lower levels than are shown on this graph, and would have been rising between then and 13:00 hours, when the next level was measured. It is easy to project back to the likely level that would have been achieved at 6 am by a simple linear regression analysis. This is shown for urea in Figure 2.

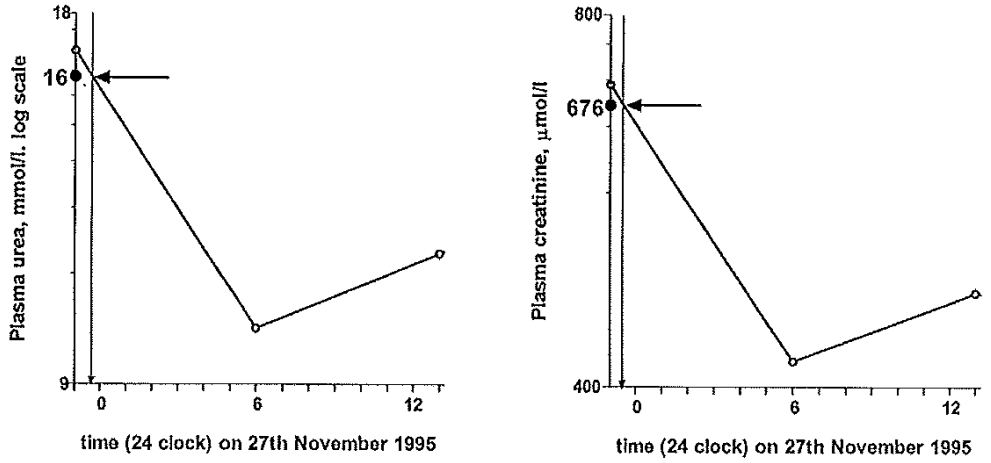
Figure 2 Linear least-squares regression analysis, showing projected

previous urea levels. It would have been approximately 10 mmol/l at 6 am.



Using this method allows us to plot the likely profile of the urea and concentrations. However, dialysis removes chemicals down their concentration gradients, and so the fall in concentration during dialysis is not linear, but a single order logarithmic decline ($1-e^{kt}$). This means that the concentration of each chemical will fall more quickly initially, and the rate of removal will then slow in parallel with its fall. For this reason, I have plotted the likely falls in natural logarithm plots (Figure 3). On these, I have also plotted the value for the newly identified specimen on the vertical axis as a solid dot.

Figure 3 Projected urea and creatinine concentrations during dialysis on Natural Log scales, with the values for the newly identified blood sample plotted. The arrows indicate the likely times of sampling.



In both cases, it appears most likely that these samples were taken shortly after the onset of dialysis, probably just before or around mid-night on 26/11/95. This may appear a bizarre time for them to be taken, shortly after the first bloods were taken. A possible explanation may be that one doctor may not have been certain that the first sample had been sent, and repeated them unwittingly.

Another common scenario that I have encountered in clinical practice is that a doctor may take a blood sample and send it to the lab, and on phoning for an urgent result may be told that the first sample had not yet arrived. Fearing it may be lost within the system (portering services, etc), the doctor may then take a second 'insurance' sample if the child has a cannula (as Adam did at that time), which means it would not be painful for the child. Typically, the laboratory then run and phone the result of the first sample as soon as it arrives, and then run the second sample but do not report it by phone as they know it is not relevant to the child's care.

In conclusion, I cannot be certain what went on in detail that night, but the newly identified sample results were taken shortly after dialysis began, and may well have been an 'insurance' sample taken before the first sample was identified as arriving in the laboratory, or similar.

What was the 'true' plasma sodium shortly before midnight on 26/11/95?

The reproducibility of plasma sodium assays is approximately ±2%, or approximately ±3 mmol/l on a typical human plasma sample. This means that if the true plasma sodium in plasma was 140 mmol/l, and if this was repeatedly measured, 95% of the results would fall in the range of 137 to 143 mmol/l, with most of the results bunching closely around the 140 value, but occasional ones being 136 or less, and an equal number of occasional ones being 144 or greater.

Thus, if the reading of the first sample had been 139, it had a 95% chance of being from a plasma whose true level was as high as 142 or as low as 136. Similarly, if the newly discovered sample, taken just after, had a result of 133 mmol/l, this could have been from a blood sample with a true value as low as 130 or as high as 136 mmol/l.

It is therefore possible for Adam's true plasma sodium to have been 136 mmol/l between 11 pm and mid-night, and for it to have been sampled and measured twice and to return values of 139 and 133.

Equally, it could be that the number telephoned by the lab was 134 for the first sample, and that it was written ambiguously to look quite like 139, but more clearly when it was entered correctly onto the flow sheet at 134. If this had been the case, the second blood test result of 133 would be intuitively recognised as 'the same value' as 134 without having to understand the statistics of laboratory repeatability.

What are the implications for Adam's pre-operative sodium, and subsequent clinical course?

For all of the reasons already explained in detail in this and my previous reports, I do not think that the uncertainty about the plasma sodium at the beginning of dialysis makes any difference to my analysis of Adam's subsequent clinical course. Whether it had started at 133 or 139, or any value in-between, his post-dialysis plasma sodium would not have been especially low, and his dramatic development of hyponatraemia must have occurred in the ensuing hours, that is after he left the ward to go to the operating theatre.

Expert Witness Declaration

I Malcolm Coulthard DECLARE THAT:

1) I understand that my duty in providing written reports and giving evidence is to help the Court, and that this duty overrides any obligation to the party by whom I am engaged or the person who has paid or is liable to pay me. I confirm that I have complied and will continue to comply with my duty.

2) I confirm that I have not entered into any arrangement where the amount or payment of my fees is in any way dependent on the outcome of the case.

3) I know of no conflict of interest of any kind, other than any which I have disclosed in my report.

4) I do not consider that any interest which I have disclosed affects my suitability as an expert witness on any issues on which I have given evidence.

5) I will advise the party by whom I am instructed if, between the date of my report and the trial, there is any change in circumstances which affect my answers to points 3 and 4 above.

6) I have shown the sources of all information I have used.

7) I have exercised reasonable care and skill in order to be accurate and complete in preparing this report.

8) I have endeavoured to include in my report those matt ers, of which I have knowledge or of which I have been made aware, that might adversely affect the validity of my opinion. I have clearly stated any qualifications to my opinion.

9) I have not, without forming an independent view, included or excluded anything which has been suggested to me by others, including my instructing lawyers.

10) I will notify those instructing me immediately and confirm in writing if, for any reason, my existing report requires any correction or qualification.

11) I understand that;

- 11.1) my report will form the evidence to be given under oath or affirmation;
- 11.2) questions may be put to me in writing for the purposes of clarifying my report and that my answers shall be treated as part of my report and covered by my statement of truth;
- 11.3) the court may at any stage direct a discussion to take place between experts for the purpose of identifying and discussing the expert issues in the proceedings, where possible reaching an agreed opinion on those issues and identifying what action, if any, may be taken to resolve any of the outstanding issues between the parties;
- 11.4) the court may direct that following a discussion between the experts that a statement should be prepared showing those issues which are agreed, and those issues which are not agreed, together with a summary of the reasons for disagreeing;
- 11.5) I may be required to attend court to be cross-examined on my report by a cross-examiner assisted by an expert;
- 11.6) I am likely to be the subject of public adverse criticism by the judge if the Court concludes that I have not taken reasonable care in trying to meet the standards set out above.

12) I have read Part 35 of the Civil Procedure Rules and the accompanying practice direction including the "Protocol for Instruction of Experts to give Evidence in Civil Claims" and I have complied with their requirements.

13) I am aware of the practice direction on pre-action conduct. I have acted in accordance with the Code of Practice for Experts.

Statement of Truth

I confirm that I have made clear which facts and matters referred to in this report are within my own knowledge and which are not. Those that are within my own knowledge I confirm to be true. The opinions I have expressed represent my true and complete professional opinions on the matters to which they refer.

Signed  Dr Malcolm Coulthard

Dated _____ 11/11/2011

Dr Malcolm Coulthard, BSc, MB BS, DCH, FRCP, FRCPCH, PhD

APPENDIX 1 Adam's perioperative fluid balance. (Assumes weight of 19 kg; surface area = 0.8 m²) Dr COULTHARD

Adam's usual daily intake (known)	Enteral intake = [2100] **ml**		
Adam's usual daily output (estimated)	Urine output = [1500] ml; insensible loss = [240] ml; dialysis loss = [up to 292] ml; faecal loss = [68] ml. **Total = [2100] ml**		
	Time between ward admission & start of preoperative fasting 2200-0500 = 7 h	**Time between start of preoperative fasting period & anaesthesia 0500-0700 = 2 h**	**Time between induction of anaesthesia & start of surgery 0700-0800 = 1 h**
Fluid losses			
a) Insensible losses	[300] ml/m²/d = [10] ml/hr = 70 **ml**	[300] ml/m²/d = [10] ml/hr = 20 **ml**	[300] ml/m²/d = [10] ml/hr = 10 **ml**
b) Urine output	[62] ml/h = 434 ml	[62] ml/h = 124 ml	[62] ml/h = 62 ml
c) Blood loss	0 ml	0 ml	0 ml
d) Dialysis loss	**Likely to be much less than 292 ml: *See Note B**	0 ml	0 ml
Total fluid losses	**Between 500 and 800 ml, most likely approximately 600 ml. *See Note B**	**144 ml**	**72 ml**
Actual fluid input	**952 ml**	**0 ml**	**750 ml**
Est. fluid (+ =excess; - = deficit)	**+152 to +452 ml**	**-144 ml (cumulative =+8 to +308)**	**+678 ml (cumulative =+686 to +986)**
Comments + Estimated SODIUM BALANCES	**Input**=Dioralyte; 953 ml = 57 mmol Na^+ **Output**=Insensible Na approximately 0, + urine likely to be 75/l = 33 Na loss, + dialysis likely to be 130/l = <38 Na loss. **Na balance**=Less than 14 mmol deficit (PD loss likely to be much less than 38, so probably in POS Na balance)	**Input**= 0 mmol Na^+ **Output**=Insensible Na approximately 0, + urine likely to be 75/l = 9 Na loss. **Na balance**= -9 (Thus, cumulatively, likely to be overall approximately 0, ie, WENT TO THEATRE IN SODIUM BALANCE)	**Input**= 31 mmol/l = 23 mmol Na^+ **Output**=Insensible Na approximately 0, + urine likely to be 75/l = 5 Na loss. **Na balance**= +28 (If accept arrival in theatre in approx Na balance, now cumulative Na balance = +28 ml)
Reasons why planned fluid infusion (content or infusion rate) should change due to change in estimated loss	• Overall, the estimated water balance pre-op is close to ZERO from +12 to 312 ml • Overall, the estimated Na balance pre-op is also quite close to ZERO, given the unknowns including the UF value and the urine sodium concentration. • It is therefore reasonable to assume that Adam went to theatre in approximately normal salt and water balance.		The cumulative Na and water balance since induction of anaesthesia, assuming he was in balance on arrival in theatre, IS: Water = +678 Na = +28 The concentration of the accumulated fluid therefore = 28/678 = 41 **mmol/l.**

APPENDIX 1 Adam's perioperative fluid balance. (Assumes weight of 19 kg; surface area = 0.8 m^2) Dr COULTHARD

	Time from start of surgery until vascular clamps on (0800-1000)	Time while vascular clamps applied (1000-1030)	Time from when clamps released until end of surgery (1030-1130)	Time from end of surgery until arrival in ICU (1130-1215)
Fluid losses				
a) Insensible losses	20 ml	5 ml	10 ml	7 ml
b) Urine output	up to 124 ml *See Note A	up to 31 ml *See Note A	up to 62 ml *See Note A	up to 46 ml *See Note A
c) Blood loss	600 ml	200 ml	328 ml	0 ml
Total fluid losses	up to 744 ml *See Note A	up to 236 ml *See Note A	up to 400 ml *See Note A	up to 53 ml *See Note A
Actual fluid input	2300 ml *See Note C	200 ml *See Note C	250 ml *See Note C	0 ml *See Note C
Estimated fluid excess	+1556 ml (cum =+2242 to +2542)	-136 ml (cum =+2106 to +2406)	-150 ml (cum =+1956 to +2256)	-53 ml (cum =+1903 to +2203)
Comments + Estimated SODIUM BALANCES	**Input** = 226 mmol Na^+ **Output**= blood 78 *See Note D + urine = approx 9 mmol total. **Na balance**= +139	**Input** = 26 mmol Na^+ **Output**= blood 26 *See Note D + urine = approx 2 mmol total. **Na balance**= -2	**Input** = 33 mmol Na^+ *See D **Output**= blood 43 *See Note D + urine = approx 5 mmol total. **Na balance**= -15	**Input** = 0 mmol Na^+ **Output**= urine = approx 4 mmol **Na balance**= -4
Reasons why planned fluid infusion (content or infusion rate) should change due to change in estimated loss	The cumulative Na and water balance since induction of anaesthesia, carrying forward the 07:00 to 08:00 values above, is therefore: • Minimum water excess = +1956 • Sodium excess = +150 • The concentration of the accumulated fluid therefore = maximum of 150/1948 = 77 mmol/l. • This is equivalent to retaining 1071 ml of fluid with a physiological Na concentration of 140 mmol/l AND AN EXTRA 885 ml of WATER.			

Appendix 2 TABLE FOR PAEDIATRIC RENAL TRANSPLANT
Showing the involvement of personnel in the various phases

Phase of the transplant process	Paediatric nephrologist	ward staff	ICU staff	Anaesth -etists	Surgeons	Scrub nurse	Runner
1. Transplant option first mentioned to family	+						
2. Transplant surgery consent process started; risks/benefits explained	+				+		
3. Preoperative preparation on evening of admission; consent confirmed	+	+		+	+		
4. Preoperative preparation 1; fasting, i.v. fluids; blood tests; dialysis	+	+					
4 (a) Preoperative preparation 2; ultra sound of neck re: CVP line	+			+			
5. Preparing theatre for start of surgery/check monitors & equipment				+			
6. Preparing donor kidney					+	+	
7. Patient arrival in operating theatre; i.v. inserted; anaesthesia induced				+		+	+
8. Insertion epidural, arterial and CVP lines; x-ray of the CVP line				+		+	+
8 (b). Insertion urethral catheter				?	?	?	
9. Pre-transplant phase of surgery				+	+	+	+
10. Vascular and ureteric anastomoses performed; ureteric and/or suprapubic catheter inserted				+	+	+	+
11. Post-transplant phase of surgery including wound closure				+	+	+	+
12. Post-surgery; anaesthesia stopped; drapes removed; drains connected				+		+	+
13. Child transferred to ICU							
14. Communicating child's condition at end of surgery to parents	+		+		+		
15. Communicating child's death to parents	+		+	+	+		