Witness Statement Ref. No. 002/3

NAME OF CHILD: Adam Strain

Name: Maurice Savage

Title: Professor

Present position and institution:

Retired 31st July 2011. Previously Consultant Paediatric Nephrologist, Royal Belfast Hospital for Sick Children/Royal Hospitals Trust, and Professor of Paediatrics, Queen's University Belfast.

Previous position and institution:
[Since your Witness Statement of 14th April 2011]

Membership of Advisory Panels and Committees:
[Identify by date and title all of those since your Witness Statement of 14th April 2011]

Previous Statements, Depositions and Reports:
[Identify by date and title all those since your Witness Statement of 14th April 2011]

A revised answer to Question 18 (a-d) in relation to Witness Statement 002/2 has been submitted (Ref. HYP B04/1) giving documented details of how, in 1995-96, Dr Savage became aware of the possibility of other hyponatraemia related deaths associated with renal transplantation in children and his subsequent actions.

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

Ref:	Date:	
011-001	28.11.1995	Draft Statement
011-015	21.06.1996	Deposition to the Coroner
002/1	22.07.2005	Inquiry Witness Statement
093-006	08.05.2006	PSNI Witness Statement
002/2	14.04.2011	Second Inquiry Witness Statement

Maurice Savage 28/9/11

IMPORTANT INSTRUCTIONS FOR ANSWERING:
Please identify clearly any document to which you refer or rely upon for your answer. If the document has an Inquiry reference number, e.g. Ref: 049-001-001 which is 'Chart No.1 Old Notes', then please provide that number. If the document does not have such a number then please provide a copy of the document.

I QUERIES ARISING OUT OF YOUR SUPPLEMENTAL WITNESS STATEMENT

With reference to your witness statement dated 14th April 2011, please provide clarification and/or further information in respect of the following:

(1) Answer to Question 1 at p.2:

"Over the period 26-28 November 1995 I was employed jointly at the Royal Belfast Hospital for Sick Children by the NHS and by Queen's University Belfast as a joint clinical appointee. This meant that I had an equal commitment to the Medical School and to the Children's Hospital. Prior to October 1995, I was the only Paediatric Nephrologist in Northern Ireland and so my primary clinical responsibility was to children with kidney disease. On the weekend, including Sunday 26 November, I was the Consultant Paediatric Nephrologist on call. On Monday 27 November I passed care for my clinical patients to my consultant colleague in order to undertake work in the University and because I had been on call over the weekend."

(a) State when you first knew that you would not be available for the entirety of Adam's renal transplant surgery due to your university commitments.

I had been on call for the weekend in question. The clinician on call for the weekend hands over to the person on call at 9.00am on Monday morning and I would have been aware of the situation during the weekend.

(b) State when you first made arrangements to pass care of Adam to Dr. Mary O'Connor in order to provide cover for Adam's surgery whilst you could not be there.

I handed over to Dr O'Connor at approximately 9.00am on the Monday morning, but planned to remain on the Royal Hospital site at my University office.

(c) In relation to your *"work in the university"* on 27th November 1995 state:

(i) at what time you were obliged to commence and finish that work

9.00am to 5.00pm

(ii) the location where you were obliged to carry out that work and the proximity of that location to the operating theatre

I worked in the Child Health office in the Clinical Institute, approximately 200 metres from the Children's Hospital and the operating theatre. The office was situated in the Clinical Institute near the Grosvenor Road entrance to the Royal Hospitals site.

(iii) the nature of that work.

My work for the University involved teaching, research and administration.

(d) If you had not had any university duties on the morning of 27th November 1995, state whether you would have remained in the operating theatre past 09.00 and/or returned to the operating theatre before closure of the wound. If so, state how long you would likely have remained in theatre, how often you would likely have returned to theatre and in both cases explain the purpose thereof. If it would have made no difference to your presence in the theatre whether you had university duties or not, explain the reasons why.

If I had not had other commitments on that morning, it is possible I would have remained at the Children's Hospital and kept regular contact with the operating theatre to be present after the vascular clamps were released. It was my practice to be available to the theatre team as the Nephrologist on call to answer any clinical queries relating to the patient undergoing surgery. Having been on call over the weekend, I handed over to Dr O'Connor to be present.

(e) Explain the reasons, on each occasion, for your presence in the operating theatre during Adam's transplant procedure

My reasons for being present in the operating theatre during Adam's transplant procedure was so that members of the surgical or anaesthetic team could obtain any information regarding his clinical condition at short notice and also so that I could communicate with his mother as to how the procedure was proceeding.

(f) The British Paediatric Association produced a report in September 1995 entitled 'Tertiary Services for Children & Young People'. That report stated (at p.66) that the Northern Ireland nephrology service was not formally recognised at the time and 'some aspects were poorly developed.' Explain:

(i) What implications, if any, the lack of such recognition had
(ii) Whether you agreed with the report that some aspects were poorly developed and, if so, what those aspects were

This report was a review of the then position and future needs for tertiary services for young people in the UK and provided "A guide for the purchase, provision and planning of specialist services for sick children." It points out that "during the previous 20 years, a number of paediatric services had developed within the discipline of paediatrics". "Before these services developed, children were treated mainly by general paediatricians, adult specialists or a combination of both. Results of treatment for some children and babies with life threatening diseases were poor, with high levels of morbidity and mortality. This led to a view that certain treatments, such as organ transplant, should not be offered to children". (page 5). Advances in both general and specialist care were rapid in the decade up to 1995 with the development of relatively new children's specialist services. In this context, the report points out those units in England were set up with regional and super-regional funding, but in Wales and Northern Ireland these children's services were not formally recognised or funded. In consequence, it suggests some aspects of the services are poorly developed.

In Northern Ireland, this was already recognised and action to address deficiencies was in

process. For example, on page 69 of the report, it points out the need for 3 consultants in each centre, with an immediate and urgent need for 2 more paediatric nephrology posts to increase the number at The Royal Free and in Belfast from 1 to 2, and for a further 8 posts across the country. The appointment of Dr Mary O'Connor in October 1995 was in recognition of this need as a result of an earlier review of renal services. Subsequently, a second report on the future of renal services in Northern Ireland recommended the funding of a full service with specialist children's renal nurses, specialist dietary support, clinical psychology input and the full funding of haemodialysis and peritoneal dialysis equipment. (Renal Services Review 2002, DHSSPSNI Ref: 20/2003, page 65-71) (See Appendix [1]).

(g) If you had not been *"the Consultant Paediatric Nephrologist on call"* when the offer of the kidney was made for Adam, what would have happened about transplant arrangements and who was the Consultant who would have been responsible for making arrangements for Adam's renal transplant in those circumstances

If I had not been the Consultant Paediatric Nephrologist on call when an offer was made for Adam, the offer would have been made to my colleague Dr O'Connor, since we alternated on call duties.

(2) Answer to Question 2 at p.2:

"When I was informed that a potential kidney was available for Adam Strain on 26 November 1995, I identified that the facility to perform the transplant was available in terms of a surgical and anaesthetic team, theatre time and a potential bed in the paediatric intensive care unit post surgery. Then I informed his mother of the offer of the kidney and verified that she was willing to allow the transplant operation. I arranged for Adam to be brought in to hospital, to provide a blood sample for the tissue typing laboratory in order to carry out a tissue cross-match and establish if the kidney was suitable. I also had to assess that Adam was clinically well enough to receive a kidney transplant and to carry out the requisite checks as laid down in the kidney transplant protocol, to arrange for the appropriate investigations to be made and to communicate Adam's medical history and current clinical condition to the surgical and anaesthetic teams involved. Once the transplant cross-match confirmation was received I discussed the management of Adam in relation to his oral intake and fluid prescription with the consultant anaesthetist. I instructed my junior medical and nursing colleagues on how the patient should be managed until such time as he left for theatre. I obtained written consent for the surgery to proceed from Adam's mother.

I communicated the details of Adam's clinical history to the transplant surgeon and anaesthetist and was involved in discussions as to the optimal time to commence surgery. Once Adam was in theatre, I checked with the consultant anaesthetist that there were no immediate problems and no issues which he needed to further discuss with me in regards to Adam's clinical care. Once the care of our patient was passed to the theatre team, I made it clear that I was available should they need to consult with me or my consultant nephrology colleague who was available whilst I left to undertake University work."

(a) Describe and explain the plan for the arrangement and conduct of Adam's renal transplant, including:

(i) when the plan was formulated

The plan was formulated on the evening of 26th November when the UK Transplant

Service indicated that there was a potential kidney available.

(ii) the identity of those involved

The plan was formulated by myself in consultation with the transplant surgeon on call and the Consultant Anaesthetist on call, Mr Patrick Keane and Dr Bob Taylor.

(iii) what was considered and included in the plan

The first consideration was that Adam's mother was prepared to allow Adam to have transplant surgery rather than continue with dialysis as renal replacement therapy.

The plan was as described in the answer to Question 2 of page 2 in my Witness Statement 002/2:

- Confirmation that Adam's mother was prepared to allow Adam to proceed to transplant surgery
- The transplant surgeon on call was identified and informed of the possibility of a transplant. Clinical details of Adam's underlying diagnosis and the information regarding the kidney on offer provided by the UK Transplant Service would have been communicated
- The Consultant Anaesthetist on call was identified and informed of the possibility of a kidney transplant needing to be performed and Adam's underlying problems identified
- The operating theatre and Paediatric Intensive Care Unit were informed of the possibility of a paediatric transplant being performed so they could make suitable arrangements
- Adam was then brought to hospital and a blood sample obtained for the Tissue Typing Laboratory so that they could carry out a tissue cross-match
- Adam was examined to ensure there was no intervening clinical developments, such as an infection, which might preclude proceeding to transplant surgery
- The pre-requisite investigations on the Transplant Protocol were then to be performed by the junior medical staff
- When the transplant cross-match was available and satisfactory, the transplant surgeon and anaesthetist were informed, so they could make specific arrangements for the surgical procedure
- Adam's fluid intake and dialysis regime were prescribed for the interim period between cross-match result and the time when he would proceed to theatre
- Written consent for the surgery was obtained from Adam's mother

(iv) what Adam's mother was told about it prior to his transplant surgery

The exact detail of what Adam's mother was told prior to his transplant surgery is not recorded, but the suitability of the kidney in terms of tissue match, the age of the donor, the process of going to theatre, the potential length of time in theatre, detail of the anaesthetic and analgesia to be provided, would have been discussed. Prior to signing the consent form, the likelihood of success of the transplant, the potential risk of such major surgery and the need for intensive care management post-operatively would also have been discussed. It is likely that she was informed of the name of the Transplant Surgeon, the Paediatric Consultant Surgeon and the Consultant Anaesthetist.

(b) State whether, when you "*informed his mother of the offer of the kidney*", you were aware of the composition of the anaesthetic and surgical team.

When I first informed Ms Strain of the offer of a kidney for Adam, I would have already checked that a Consultant Transplant Surgeon and a Consultant Anaesthetist were available to perform the transplant. The full composition of the anaesthetic and surgical team may have been decided at a later stage by the Consultant Anaesthetist and Transplant Surgeon, including the involvement of a Paediatric Consultant Surgeon. I cannot be certain of the exact chronology of events 16 years ago.

(c) State when Adam was first placed on the renal transplant list

I believe Adam would have been placed on the renal transplant waiting list shortly before or at the time he commenced on dialysis treatment in November 1994.

(d) State when you first discussed the need for renal transplantation with Adam's mother

I would have first discussed the need for renal transplantation with Adam's mother in early 1994 when it became apparent that he would need some form of renal replacement therapy and before he commenced on dialysis treatment. A renal transplant On-Call information booklet was provided (058-012-037).

(e) When you first discussed the need for renal transplantation with Adam's mother:

(i) State what you believed was the realistic estimate of the chances of a functioning graft:

- immediately
- after 1 year
- after 3 years
- after 5 years

When it became apparent that Adam would need a renal transplant, I would have explained that the chances of a kidney transplant functioning immediately were 90% and that the maximal risk of a kidney failing would be in the first month and then in the first year. It is not likely that I would have given specific estimates of chances of a functioning graft after 1, 2 and 5 years, but I would have been more likely to have indicated that I would have expected a 60-70% 10 year graft survival or better. I believe our current 5 year survival rate then was around 60%.

(ii) State if you discussed those estimates with Adam's mother; if not, explain why not

I would have discussed such estimates with Adam's mother but cannot be certain of the detail.

(f) State if you discussed the disadvantages of transplantation with Adam's mother. If so, state what disadvantages you discussed. If not, explain why not

I did discuss the pros and cons of transplantation versus long-term dialysis with Adam's mother. The major disadvantages were of course the risk of major surgery to his life, the risk of a kidney failing at an early stage making subsequent transplants more difficult, both technically and because of tissue sensitisation, but given difficulties of maintaining small children on dialysis, I am sure that we discussed the fact that a good functioning graft would

give Adam the best chance of a normal childhood.

(g) Explain how you *"verified that [Mrs Slavin] was willing to allow the transplant operation"*, and what was discussed at this time in terms of:
(i) the risks and disadvantages of the transplant surgery with this donor kidney
(ii) the risks and disadvantages of not pursuing the surgery at this time

I talked to Adam's mother on the telephone, to re-confirm previous discussions and decisions that we would proceed to a kidney transplant if a suitable kidney was offered. I cannot be sure after this passage of time of the exact detail of that discussion in terms of the risks and disadvantages of transplant surgery with this particular donor kidney, as opposed to not pursuing the surgery. It is more likely that I further discussions with Mrs Slavin when she came to hospital.

(h) Identify where in Adam's notes you recorded your discussions with Ms. Slavin leading to her *"verifiying] that she was willing to allow the transplant operation"* . If you did not make such an entry in Adam's notes, explain why.

I do not believe I entered details of such discussions in the notes. I had a strong relationship with Adam's mother and I believed that we were both agreed that despite the risks of surgery, a transplant was Adam's best chance of achieving a normal life.

(i) Describe the actions and *"requisite checks"* carried out *"as laid down in the kidney transplant protocol"*.

Requisite checks are listed in the Renal Transplant Protocol which I have previously provided.

In terms of medical history this included a review of his residual renal function, urine output, recent infections such as urinary tract infections and peritonitis, recent contact with infectious disease, and a review of the patient's current drug therapy.

Examination would include an estimation of state of nutrition and hydration, blood pressure, measurement of height and weight, and a check on the peritoneal dialysis catheter exit site.

Investigations would include blood sampling for a tissue cross-match for grouping and cross matching 4 units of blood, for estimation of a full blood picture and white cell count, urine and peritoneal dialysis fluid for culture, a blood sample for urea and electrolytes and for virology.

The Transplant Surgeon, Paediatric Surgeon, Anaesthetist, theatre and Intensive Care Unit would be contacted. A check that parents had a copy of the Transplant Booklet, and an assessment as to whether fluid restriction caused by pre-operative fasting required intravenous fluids would be made.

(j) State whether, by 26th November 1995, you had discussed the fluid protocol from Bristol with Dr Mary O'Connor, and if so, what you discussed, when you discussed it, and the outcome of that discussion.

I cannot say after this time if Dr O'Connor and myself had discussed in detail the fluid protocol from Bristol by 26th November, but it would certainly have informed our subsequent

practice and the content of a new protocol in 1996 (provided in Appendix [2]), including recommendations on the type of IV fluids to be used intra-operatively. I am aware we discussed and decided to change to the Bristol immunosupression recommendations.

(k) State whether the RBHSC has a system for incorporating new guidance. If so, please describe it and identify any document in which it is incorporated, and state when it came into effect.

The Belfast Trust now has a Standards and Guidelines process. An example of how this operated in relation to Hyponatraemia Guidelines is provided in Appendix [3].

(l) State whether the *"oral intake and fluid prescription"* which you discussed the night before surgery with *"the consultant anaesthetist"* was the same as the actual intake of fluids that Adam received.

The oral fluid intake and fluid prescription which I discussed on the night before surgery with the Consultant Anaesthetist was affected by the fact that IV access was lost during the course of the night in question. As a result Adam got some 500mls less fluid than was originally planned. His total fluids overnight were 970mls.

(m) State whether you believe the *"oral intake and fluid prescription"* discussed was correct with hindsight.

I believe the oral intake and fluid prescription originally discussed was correct.

(n) Identify by name and job title your *"junior medical and nursing colleagues"* whom you instructed on how the patient should be managed, and state the instructions given.

I do not know the identity of the nursing staff in question that night. I now believe the junior doctors on call that night have been identified as Dr Cartmill and Dr O'Neill.

The instructions in relation to Adam's overnight peritoneal dialysis which he normally had at home was that this was to be set up as usual, in other words, he was to have 750ml volume cycles with 15 cycles given over 13 hours on a normal evening. This regime was to be followed but the dialysis was to stop and his abdomen drained shortly before going to theatre. This meant that Adam would only have 7-8 hours dialysis on that night. In relation to Adam's gastrostomy tube feeds, normally he received 1500mls overnight of Nutrison, a high calorie feed. Since Adam was going to theatre early in the morning at around 6.00-7.00am, I ordered that a clear fluid solution Dioralyte should be used instead, and this should be infused at 180mls per hour to give him just over 1 litre of this fluid. The balance was planned to be made up by intravenous fluids but the IV line tissued between 1.00 and 2.00am and could not be re-erected. Subsequently the volume given by gastrostomy tube was increased from 180mls an hour to 200mls an hour (fluid record chart 057-010-013) as this was judged to be the maximum amount that Adam could tolerate without the volume making him sick.

(o) State what was *"the optimal time to commence surgery"*

The optimal time to commence surgery is normally as soon as possible after a satisfactory tissue match is obtained, usually within 24 hours of the kidney having been donated ie. before approximately 1.00am on 27th November.

(3) **Answer to Question 2 at p.3:**

"Once Adam was in theatre" **and you** ***"checked with the consultant anaesthetist that there were no immediate problems and no issues which he needed to further discuss with [you] in regards to Adam's clinical care"***

(a) State whether you ***"checked with the consultant anaesthetist that there were no immediate problems and no issues which he needed to further discuss with [you] in regards to Adam's clinical care"*** **before or after IV access was established in theatre.**

Yes, I did check with the Consultant Anaesthetist that there was no issue or information which he needed to discuss with me once Adam was anaesthetised and before surgery was commenced. I believe IV access would have been established at that time.

(b) State whether you discussed at any time the agreed plan that a blood sample for electrolyte and urea estimation be sent to the laboratory once IV access was established in theatre. If so, state the nature of the discussion. If not, state the reasons why you did not discuss it.

When IV access could not be obtained in the early hours of the morning of the 27th November, I understand that the Anaesthetic Registrar was called in an effort to obtain such IV access and he held discussions with Dr Taylor. I understand that a decision was made not to pursue repeated efforts to obtain IV access because of the distress caused to Adam. The anaesthetic team decided to delay IV access until Adam was asleep. I requested that the urea and electrolyte estimation, which I had previously asked to be sent prior to him going to theatre, would then be sent immediately from theatre and indeed I believed this had been carried out.

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

"By March 1994 it became apparent that the only realistic chance for long-term survival for Adam was through renal replacement therapy and this was discussed with his mother. It was agreed that he would start on peritoneal dialysis and that we would seek a kidney for transplantation. My role then extended to managing his peritoneal dialysis and ensuring that his mother was prepared, trained and capable of performing home peritoneal dialysis. This preparation and training involved a renal nurse specialist who undertook the training and assessed the home situation as being suitable for dialysis and signed off Adam's mother's competency in the procedure.

Once renal replacement therapy was required, I established Adam's blood group and tissue type and arranged for him to be put on call for a cadaveric renal transplant. I was responsible for carrying out the appropriate preparatory investigations and explained to his mother what this major surgery involved and confirmed that she was prepared to consent to the procedure."

(a) As part of the ***"preparatory investigations"*** **state whether you:**

(i) Considered conducting an ultrasound examination of the veins in Adam's neck to identify those which remained patent and

I did not consider conducting an ultrasound examination of the veins in Adam's neck as I had no reason to believe they were not patent. As a result of our experience with Adam Strain, we now routinely carry out pre-operative ultrasound flow studies of neck veins in children who have had previous neck intravenous lines.

(ii) Considered assessing Adam's central venous access for this surgery and formulating a strategy for this
- If you did consider either of those steps, state when you considered them.
- If you did not consider such action, explain the reason why

Because I had no reason to believe there was a problem with central venous access and had not encountered such a problem in other patients, I did not formulate such a strategy. These central venous lines are placed by anaesthetists and if there had been a problem identified in theatre, I believe a Doppler study could have been performed at that stage. As a result of our experience with Adam Strain we would now carry out flow studies pre-operatively on any vessels previously cannulated which might be involved in the procedure.

(iii) Discussed with Dr Taylor a strategy for Adam's central venous access for this surgery and the monitoring of Adam's central venous pressure during surgery. If so, describe in detail your discussion. If you did not discuss this, explain the reasons why not

I would have discussed with Dr Taylor the need for a multiple lumen central venous line for central venous pressure monitoring during surgery and for use to provide intravenous fluids and intravenous drugs post-operatively.

(iv) Discussed with Dr Taylor the problems that might be faced in trying to insert a central venous catheter into Adam, and whether he wanted preoperative ultrasound scanning of Adam's neck.
- If you did discuss this, state when you discussed this and what problems you discussed.
- If you did not discuss this, explain why.

As stated above, I had no reason to believe there might have been a problem with central venous access and this was not an issue that was raised with me by Dr Taylor in discussion.

(b) Describe what you told Ms. Slavin when you *"explained to [her] what this major surgery involved"*.

I would have explained to Ms Slavin not only on the occasion of Adam being brought for a potential transplant, but on previous occasions, the nature of the major surgery involved ie. that he would require his abdomen to be opened and that the vessels from the transplanted kidney would be attached to intra-abdominal vessels carrying blood to and from the leg. I would have explained that connecting the donor kidney vessels to these vessels ran the risk of bleeding, but to prevent this, vessels would be clamped and while the surgery was completed, it would checked there was no bleeding from the join (anastomosis). I would also have explained that the ureter tube from the transplant kidney would need to be attached to Adam's bladder. I would have explained that he would need to have a bladder catheter placed and I would have explained that he would have required a long intravenous

neck line.

(c) Describe the options you offered to Ms. Slavin in terms of the venue of the transplant surgery when you "*confirmed that she was prepared to consent to the procedure*".

As there was only one venue for transplant surgery in Northern Ireland for a child of Adam's age, I did not offer Ms Slavin any other venue for the transplant.

(d) Identify where in Adam's notes you recorded:

(i) The discussions with Ms. Slavin giving rise to her providing the confirmation of her "*consent to the procedure*" to which you refer. If you not make such an entry in his notes, explain why.

I am unable to identify in Adam's notes any recording of the discussions which I had with Ms Slavin in relation to obtaining consent, nor in relation to the detail of the transplant surgery. I have no doubt however that I did spend a considerable time discussing these issues and that these discussions were full and frank.

(ii) Any of your discussions with Ms. Slavin in relation to Adam undergoing renal transplant surgery. If you did not make any such entries in his notes, explain why.

It was not my habit at that time to make such detailed notes, but would now be standard practice. Modern consent forms now require the list of potential complications discussed to be recorded. This was not so in 1995.

(e) State whether you considered arranging for a paediatric renal transplant surgeon to be involved in the:

(i) Assessment of Adam for placement on the transplant list
(ii) Discussion with Ms. Slavin prior to placing him on the transplant list
(iii) placing of Adam on the transplant list
If so, state your reasons and explain what action you took in the light of it. If not, explain why you did not consider it.

I did not consider arranging for a Paediatric Renal Transplant Surgeon to be involved in the assessment of Adam for placement on the transplant list in discussions with Ms Slavin prior to placing Adam on the transplant list. There is no specific Paediatric Renal Transplant Surgeon in Northern Ireland and, as in many other units at that time and indeed now, this type of surgery which is extremely specialised is carried out by transplant surgeons who generally have an adult background. It is now our practice for a transplant surgeon to be provided with a clinical summary of children going on call for a kidney transplant and for the surgeon to meet the child and family in advance of surgery.

(f) State if you were aware, as at the time of Adam's transplant surgery, of any protocol, guidance or procedure on the gaining of consent generally, and specifically in relation to renal transplantation. If so, identify it and state whether it had any impact on your actions in relation to Adam.

I am not aware if at the time of Adam's transplant surgery there was a protocol or guidance for gaining consent generally or specifically in relation to renal transplantation.

(g) State the reasons why Mr. Keane or Mr. Brown were not involved in the formal consent process.

At the time when Adam's transplant was performed it was not always the surgeon involved who took the consent as it would be today. Only the surgeon performing an operation would sign a consent form today.

(h) State whether you think Mr. Keane or Mr. Brown should have been involved in the consent process. If so, state at what stage that should have happened and provide your reasons. If not, explain why not.

I expected that the transplant surgeon would have discussed the surgery with Ms Slavin prior to Adam going to theatre and confirmed consent and that similarly, the anaesthetist had discussed the anaesthetic with Ms Slavin. Current practice would require a transplant surgeon to meet, assess and explain the surgery when a child goes on call and to obtain consent on the occasion of the operation.

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

"Between November 1991 and April 1992 I estimate that Adam had up to ten surgical or anaesthetic procedures."

(a) State whether you had any discussions with Dr. Taylor about any of Adam's previous surgical or anaesthetic procedures prior to Adam's transplant. If so, please state when you had those discussions, what you discussed and why.

In discussions with Dr Taylor, prior to the transplant procedure on 26th November 1995 I would have discussed with him the complexity of Adam's surgical history. Indeed, it is my understanding, that Dr Taylor had been involved as the anaesthetist for his surgery on at least two previous occasions.

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

"Between 23 and 26 August 1994 Adam was again admitted for a surgical procedure; the insertion of a peritoneal dialysis cannula. This was performed by Mr Victor Boston. Immediately post- operatively, there was an episode of hypotension which was corrected with a bolus infusion of HPPF (Human Plasma Protein Fraction). Several cycles of peritoneal dialysis showed that there was blood loss in the peritoneal cavity, possibly the reason for his hypotensive episode due to an associated hypovolaemia. However, this blood cleared by the following day and 48 hours after insertion of the cannula, it was felt that he was stable, comfortable and allowed home (Ref: 057-102-180 to 182). He was readmitted a week later so that his mother could undergo training in the dialysis technique (Ref: 057-102-183 to 185). I note that during this admission when his tube feeds were discontinued because of the abdominal operation on 24 and 25 August 1994 that he received intravenous fluids at N/5 (0.18%) saline in 4% dextrose. His sodium during that period was 131 but on returning to his tube feeds his sodium was 140 on readmission on 3 September. He was at this time polyuric."

(a) Explain the significance of the fact that Adam *"received intravenous fluids at N/5 (0.18%) saline in 4% dextrose"* on 24th and 25th August 1994.

The significance of Adam receiving N/5 saline in dextrose on 24th and 25th August may be that it contributed to the fall in his serum sodium from 133 to 131. However, he was also fasted for 8 hours on 24th August which may also be a contributing factor since his sodium returned to 140 when tube feeds were recommenced.

(b) State what volume and infusion rate of 'Solution 18' was prescribed and administered on 24th and 25th August 1994 and how this compared with the volume and infusion rate prescribed for and administered to Adam between 26th and 28th November 1995. If there is a difference, please explain it.

I have examined the records and the infusion rate of 'Solution 18' administered on 24th and 25th August 1994 was 87mls per hour with a total volume of 1809mls between 1.00pm on 24th and 7.00am on 25th. Over a 24 hour period this would have equated to just over 2 litres of fluid, Adam's normal daily requirement. On 27th November 1995 Adam received 500mls of the same solution in the first half hour in theatre and a total of 1500mls over 4 hours, a rate equivalent to almost 400mls per hour. Some of this was to compensate for the 500mls deficit in his fluid intake overnight. During the 4-5 hours in theatre, he also received a litre of HPPF, 500mls of Hartman's solution and 500mls of packed cells. I was not involved in the prescription of these volumes of fluid in theatre. While the situations are not directly comparable, I am unable to give a clear explanation for the difference of infusion rates of the number 18 Solution (N/5 saline in dextrose).

(7) Answer to Question 3(c) at p.5:

"Adam's ability to alter his urine output and urinary electrolyte losses in response to changes in his clinical condition were limited. The kidneys function in maintaining body homeostasis was severely impaired."

(a) State what ability Adam had *"to alter his urine output and urinary electrolyte losses in response to changes in his clinical condition"*, and state how this should have been factored into the fluid management of his surgery.

Adam was relatively polyuric with a urine output estimated at 50-60mls per hour. He would therefore have required fluid replacement of this volume during the course of his surgery to compensate for this. The plan to check his serum sodium and electrolytes at the start of surgery to be sure they were normal would have been a factor in deciding which intravenous fluid to use for replacement.

(8) Answer to Question 3(c) at p.5:

"Adam's serum sodium could vary from 119 (055-054-159) to 152 (050-024-220). He was however generally asymptomatic in relation to these sodium levels, most likely because they developed gradually and were corrected gradually, most often by variations in his enteral feeds. This choice of enteral feed was made in consultation with the renal dietician. Paediatric Nutrison, which we used for his enteral feeds, balanced his sodium loss reasonably consistently, and it also provided high calorie content."

(a) State whether you discussed that *'Adam's serum sodium could vary from 119 to 152'* with Dr. Taylor prior to Adam's surgery and that he was generally asymptomatic in relation to those levels *"most likely because they developed gradually and were corrected gradually"*. If so, please give your reasons for doing so. If you did not discuss it, provide your

reasons.

I believe I did discuss with Dr Taylor that Adam had developed low levels of sodium previously. I believe Dr Taylor had experience of managing children with chronic renal failure and was aware that during prolonged anaesthesia or in intensive care, special attention was required to serum sodium levels.

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

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

Attention was given to the need to maintain a similar fluid and electrolyte input to that which Adam normally received. I was aware that Adam's sodium level was normal on the evening on 26th November. When his transplant was delayed by the surgical and anaesthetic team until the following morning, I made it clear to Dr Taylor that it was important that his sodium and electrolytes were checked immediately prior to theatre.

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

- on admission on 26th November and before and after dialysis
- prior to the commencement of transplant surgery 'knife to skin'
- after the commencement of transplant surgery 'knife to skin'

I ordered that Adam's electrolytes were checked before and after dialysis, ie. prior to commencement of transplant surgery. The decision as to the frequency that the sodium needed checked subsequently would have depended on the length of the surgery and would have been decided by the Consultant Anaesthetist, although there was always a Nephrologist available for discussion during the procedure.

(c) State whether you discussed your belief that Adam's *"urine output each day was 1200 - 1500ml"* (Ref: WS 002/1, p.3) with Dr. Taylor, and state the reasons for doing so. If you did not discuss this, explain why not.

I believe I did inform Dr Taylor of Adam's urinary output. It is also possible that during transplant surgery, a bladder catheter could have been passed and the urine output measured during the procedure.

(9) Answer to Question 3(d) at p.6:

"The measurement of urine output in small incontinent children is best achieved when there is a urinary catheter in situ. Adam underwent many invasive procedures which were upsetting and on occasion frightening. To reduce his distress frequent catheterisation was avoided. The alternative is to measure urine output based on weighed nappies, ie. the difference between dry and wet weight in each nappy would be the urine output. After having established a best estimate of Adam's urine output, subsequently a fluid intake volume was based on this and allowances for other fluid losses, ie. vomiting, insensible loss and dialysis ultrafiltration."

(a) State what *"best estimate of Adam's urine output"* you established in 1995, and when and by what means you established this estimate.

In 1995, Adam was receiving 2.1 litres of fluid daily. If we accept that his insensible loss was some 300mls, and that on most days 400mls were removed during his dialysis treatment, he remained at a reasonably stable weight as measured each day. Subtracting 700 from 2100 means that we can assume that the remaining 1400mls is passed as urine.

(10) Answer to Question 3(d) at p.6:

"Preliminary urinary sodium and electrolyte measurements were performed at regular intervals to establish that there was no major variation in urinary sodium loss. Glomerular filtration rate was calculated using the Schwartz formula (height in cm x 40 divided by serum creatinine in mmol/L) from serum creatinine when required. Serum urea, creatinine and electrolyte measures were carried out on a regular basis during in-patient admissions and particularly when IV fluids were being employed and at each out-patient follow-up visit."

(a) Explain what you mean by *"regular intervals"* in relation to the *"preliminary urinary sodium and electrolyte measurement"*

(b) Explain why Adam's urinary sodium had not been measured after December 1993.

Answer to (a) and (b):

Preliminary urinary sodium and electrolyte measurements were carried out on several occasions, but I can see no record in Adam's notes after December 1993. Measurements which were made suggest that there was no major variation in his urinary sodium loss.

(c) State Adam's *"Glomerular filtration rate"* and when it was calculated.

(d) Explain what you mean by *"when required"*.

Answer to (c) and (d):

As Adam's serum creatinine rose, indicating that his kidneys were functioning less efficiently in terms of waste excretion, we would have calculated his glomerular filtration rate using the Schwartz formula. It is generally accepted that when this falls below 10 that renal replacement therapy is essential. Having established in mid-1994 that the level had been reached, renal replacement therapy was initiated. These calculations were made to establish when we should embark on dialysis.

(11) Answer to Question 3(d) at p.6:

"The plan was therefore to have regular ongoing measurements of renal function and weight. Once it was decided that Adam should start on peritoneal dialysis, this was introduced gradually on an in- patient basis to determine the optimal peritoneal dialysis regimen, ie. the volume, content and frequency, to design a prescription that would produce a stable situation when dialysis was performed at home. Volume content and frequency of the dialysis fluid and cycles were recorded in a dialysis diary, one page for each night's dialysis, including volume of fluid removed or retained and his weight before and after dialysis. Records were kept by Adam's mother and checked by the dialysis nurse specialist and/or myself both in hospital and during home visits. The volume and content of Adam's feed through his gastrostomy tube was based on estimates of his calorie and electrolyte needs and his fluid requirements. The

development of these plans was supervised by myself, in consultation with a dietician and other members of the renal team, including nursing staff."

(a) State your *"estimates of his calorie and electrolyte needs and his fluid requirements"* when Adam was admitted on 26th November 1995 and explain the basis of them.

When Adam was admitted on 26th November 1995, he would already have had his three 200ml bolus feeds of Nutrison during the day and his bicarbonate supplements. Overnight Adam would have been expected to have a further 1500mls of Nutrison tube feed which would provide him with 1200 calories and 25mmol of sodium.

(12) Answer to Question 3(h) at p.8:

"Details of Adam's peritoneal dialysis records are not available as we have not got the parent-held records on file"

(a) Identify all of the records of Adam's dialysis following his admission on 26th November 1995 and furnish copies thereof.

(b) State whether you or any nurse checked those records prior to Adam's transplant surgery, and if so state who checked the records and when and where they were checked. If the records were not checked, state the reasons why not.

Answer to (a) and (b): I have been unable to identify any dialysis records and therefore cannot be sure that any nurse checked these. Although I cannot remember, it was my practice to check these personally.

(13) Answer to Question 4(a) at p. 8:

"The reasons for the statement that Adam had a 'potential for a low sodium' was based on the fact that on several occasions he had developed a relatively low serum sodium and was known to lose sodium in his urine based on urinary electrolyte analysis and compensated for by sodium supplements in his nutritional prescription."

(a) State what was the most recent *"urinary electrolyte analysis"* used and identify the record of it.

The most recent urinary electrolyte analysis identifiable in Adam's notes is in December 1993 as you have pointed out in Question 10. I have been unable to identify any subsequent urinary electrolyte analysis. We subsequently added urine, urea and electrolyte estimation to the pre-transplant protocol (See Appendix 2).

(14) Answer to Question 4(b) at p.9:

"Adam's mother was meticulous in his care, including undertaking his gastrostomy tube feeds and giving him his medication. In doing so, she would have been aware that he had sodium bicarbonate supplements and on occasions had saline added to his Nutrison tube feeds."

(a) You have not adequately answered the question. Please state whether the *"potential for low sodium"* was discussed with Adam's mother together with *"what if any role she was to play in maintaining his sodium concentration at an acceptable level"*.

I believe that when Adam had saline and sodium bicarbonate supplements added to his Nutrison tube feeds, that we would have indicated the reason he required these supplements was to maintain his serum sodium. I believe this is supported by Adam's mother's communications with the Coroner (011-009-027).

(15) Answer to Question 4(d) at p.9:

"Adam's usual daily sodium intake before 27 November 1995 was 67mmol. 28mmol came from 1200mls of Paediatric Nutrison, 15mmol came from 100mls of normal saline and added to the Nutrison and 24mmol from his sodium bicarbonate supplement."

(a) State the volumes that Adam was receiving daily of (i) Nutrison, (ii) water, (iii) sodium, (iv) normal saline (v) any other fluids.

The answer to the original Question 4(d) at page 9 of the Statement Ref No 002/2 is based on information at 057/068. However, I believe this refers to Adam's prescription in June 1995. In fact by November, Adam was now receiving three 200mls boluses of Nutrison by day and 1500mls by continuous infusion overnight, ie. a total of 2.1 litres (note on 09/11/95 ref. 058-035-143) Paediatric Nutrison contains 23mmol per litre of sodium and Adam was also taking 12.5mls of sodium bicarbonate 4% on four occasions during the day, this provides a further 24mmol of sodium, and 100mls of normal saline providing some 15mmol of sodium. A daily total of 85mmol of sodium.

(16) Answer `to Question 4(h) at p.10:

"Adam's usual peritoneal dialysis ultrafiltration rate was approximately 400ml as indicated in a letter dated 8 June 1995 (057-056-114, 115)."

(a) Identify the entry in Adam's medical notes of his visit to the dialysis clinic on 8th June 1995.
The entry is at 057-102-191

(b) Identify the record in Adam's medical notes of his *"usual peritoneal dialysis ultrafiltration rate"*.

I believe there is no specific entry in the notes as this letter would have been dictated in lieu of a note during the clinic.

(17) Answer to Question 4(h) at p.10:

"Adam's mother was meticulous in maintaining such records in the parent-held dialysis book. The keeping of a record of both the fluid volume removed each night through Adam's peritoneal dialysis and his weight, before and after the dialysis, was part of the standard training for all parents. Its importance was emphasised as on home dialysis, electrolytes are not measured when commencing and completing dialysis. Home peritoneal dialysis training was carried out by the renal dialysis nurse and only when dialysis had been performed satisfactorily without help from nursing staff in the ward unit was the competency of the parent signed off. Initial home dialysis was performed by the parent in their home with a renal dialysis nurse present usually in another room who would be available should any problem arise. There was also ongoing telephone liaison and home visits by the dialysis nurse and checks on the dialysis

record and ultrafiltration both by the nurse and at the dialysis clinics in the hospital."

(a) You have not adequately answered the question. Please state what was discussed with Ms. Slavin about maintaining a record.

Discussion about maintaining a record would have been an integral part of the training process during which it would have been made clear as stated that the record, particularly of fluid volume retained or removed and daily weight before and after dialysis, were important. If, for instance, a child's weight rose at the same time as very little fluid was removed by the dialysis, then there would be instructions on how to change the type of dialysis fluid to counteract this. The stronger the dialysis fluid in terms of dextrose content, the more fluid it is likely to remove during a dialysis session. If on the other hand, a child's weight fell and little fluid was removed, then extra oral fluid or a lighter concentration of dialysis fluid might need to be used the following night. Specific parameters would be set and discussed between the dialysis nurse and the parent. Where there was any concern about which fluid to use and whether there needed to be any adjustment to the fluid intake, we would have discussed the need to contact the dialysis unit for advice. The maintaining of the record was therefore important and was monitored regularly by a doctor or nurse at the dialysis clinic or by telephone. As I said, Adam's mother was meticulous in maintaining the record and in contacting the hospital if she had any concerns.

(18) Answer to Question 4(h) at p.10:

"Fractional excretion rates were not measured or recorded."

(a) Explain the reasons why *"fractional excretion rates were not measured or recorded"* prior to 27th November 1995.

Fractional excretion of sodium (FENa) was not measured or recorded. It was not a test regularly utilised in this clinical situation at RBHSC, in my training experience at Great Ormond Street Hospital or at the Royal Manchester Children's Hospital. Even in recent discussion with local colleagues they confirm it is also their experience that FENa is still not a test regularly utilised in this medical situation. The use of FENa is not mentioned in the clinical reference textbook commonly used in the UK at that time, in the section on Disturbances in fluid and electrolyte balance. (Clinical Paediatric Nephrology 2nd edition 1994 pp111-117,Editor R.J. Postlethwaite, Publisher Butterworth-Heinemann ISBN 07506 1347 5).

(b) State when and explain why the measurement and recording of fractional excretion rates was introduced by the RBHSC.

The measurement of fractional excretion of sodium (FENa) has been available at RBHSC for at least 20 years. It has been more commonly used to analyse the cause of acute renal failure. I have described its use in The Handbook of Neonatal Intensive Care edited locally by Halliday, McClure and Reid , published by Balliere Tindal in 1989 (ISBN0-7020-1399-4). In children with Chronic Renal Failure it has been our practice to adjust sodium intake to correct low serum sodium levels.

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

"Following the registration for a kidney transplant on 24 November 1994, plans were made for

a transplant in the event that a suitable donor became available Adam. This included ...

The names and age of children on call were thus made known to the transplant co-ordinator, and the list circulated to all the nephrologists in Belfast and the transplant surgeons. I had a key role in formulating these plans in conjunction with the multi-disciplinary team of renal nurses, dieticians, psychologists and social workers. I as the Consultant Nephrologist along with the renal dialysis nurse, had regular discussions with Adam's parents (and possibly his grandparents) explaining the system of being on call, the nature of the surgery, the need for a tissue cross-match once a kidney was identified, the fact that the child would be called to the hospital at least six hours before the procedure for a clinical work up, and that depending on the cross-match and the agreement of the surgical team, it would then be decided if the transplant should proceed. All parents of sick children going on call for a renal transplant are given an explanatory booklet. A copy of which has previously been provided to the Inquiry."

(a) Describe what was in the *"plans"* other than the details of *"Adam's name, date of birth and tissue type"* and state where those *"plans"* are recorded.

Patients on dialysis are regularly discussed at the weekly multi-disciplinary team meeting. If it was felt there were specific needs of a child or family, a plan to address those needs would be evolved. Previous surgery or other medical problems (e.g. asthma or hypertension) which might influence the Transplant surgery would be considered. This discussion would usually involve the designation of individuals who might address such problems. In Adam's case for instance, he was later referred to a clinical psychologist because of the effect of his chronic illness on his behaviour. We would check that the transplant co-ordinator was aware of each child who was on-call, that the social worker had met with the family to identify any areas with which she could help, that the team psychologist could meet with the family to identify any stresses that she could help alleviate, and the dietician would discuss with the nurses and doctors any alteration required to the feeding regimen. At that time, no notes were made of such multi-disciplinary team meetings.

(b) State what was discussed with *"the multi-disciplinary team"* and when that discussion took place.

As described, social, psychological, dietary, medical and nursing issues would be discussed by the entire team in relation to each child who was on dialysis or who had had a transplant at the weekly meeting. There would therefore not just be one meeting where a plan was formulated, but a regular ongoing update of the needs of each child and family.

(c) Identify the persons on *"the multi-disciplinary team"* by name and their role in formulating those plans.

The multi-disciplinary team consisted of the renal nurses; the senior nurse at that time being Ms Joanne Clingan, the dietician was Mrs Janet Mercer. I cannot recall the name of our social worker 16 years ago, nor of the clinical psychologist. The two medical members of the multi-disciplinary team would have been myself and Dr Mary O'Connor.

(d) State whether any transplant surgeon formed part of *"the multi-disciplinary team"*, and if so, identify the surgeon. If not, state the reasons why not.

The transplant surgeon did not participate in these multi-disciplinary team meetings, except by special arrangement, as he worked not on the Royal Victoria site but on the Belfast City

site.

(e) Explain the purpose of the list of *"The names and age of children on call"* being *"circulated to:"*

(i) *"all the nephrologists in Belfast"*
(ii) *"and the transplant surgeons"*

The names and ages of all children on-call and indeed of all the adults on-call for kidneys was circulated to all nephrologists and the transplant surgeons each month. This was to check that individuals requiring a kidney remained active on the transplant list, particularly if they had been suspended because of inter-current illness or problems and also so that the nephrologists involved would be able to distinguish between children and adult patients. There was one, and still is, one overall Belfast list.

(f) Identify the members *"of the surgical team"* who were involved in the decision *"if the transplant should proceed"*.

The surgeon involved in a decision if a transplant should proceed would be the transplant surgeon on-call in Belfast on the day.

(g) State at what point those members *"of the surgical team"* were involved in that decision, and, in particular, state whether they were involved in the decision:

(i) Whether to accept the kidney initially from Transplant Service

When the Paediatric Nephrologist receives the offer of a kidney for a child in Belfast, it is standard practice to identify the transplant surgeon, as obviously the surgery cannot proceed unless he agrees to carry out the procedure. Factors such as the size discrepancy between donor and child, the tissue match, the current clinical condition of the patient, the underlying diagnosis would be discussed as would any particular anatomical feature of the offered kidney, which would influence the surgeon's decision as to whether to proceed or not.

(ii) Whether to confirm the decision to proceed with the transplant after the tissue cross-matching

Once the surgeon had agreed in principle that the transplant was feasible, he would be informed either by the Paediatric Nephrologist or directly by the Tissue Typing Laboratory of the result of the tissue cross-match which would clearly influence his decision to continue with the transplant, a satisfactory cross-match being mandatory.

(iii) Whether the transplant should proceed on inspection of kidney prior to commencement of anaesthesia

I believe it is normal practice for the surgeon to inspect the kidney prior to commencement of anaesthesia. Indeed, it is the transplant surgeon who normally collects donated kidneys from the Belfast City Hospital where they are first delivered. The transplant surgeon then brings the donor kidney to the Children's Hospital theatre for inspection.

(20) **Answer to Question 5(d) at p.11:**

"Following receipt of an offer of a kidney for Adam, I confirmed with UK Transplant that I felt the match was acceptable for the patient and accepted it from the Transplant Service. The kidney would then have been delivered to the renal unit in the Tower Block of the Belfast City Hospital so that samples from the tissue could be cross-matched against Adam's white cells on the BCH site where the tissue typing laboratory is situated. Subsequently, when the decision to proceed with the transplant was confirmed, the kidney was collected by the transplant surgeon and brought to the Children's Hospital."

(a) Identify *"the transplant surgeon"* who collected the kidney and brought it to the RBHSC

The surgeon was Mr Patrick Keane.

(b) State, at the time of your consideration as to whether or not to accept the donor kidney, the information that you had about that kidney, the source of that information, including identifying any relevant document.

At the time of our consideration as to whether or not to accept the donor kidney, the information I had was communicated to me by telephone from the UK Transplant Service. I was aware that the kidney came from a 16 year old donor, that the match was 3 out of 6 tissue types, but I cannot be sure that I was aware of the detail of the vascular anatomy.

(c) State what factors you considered when deciding whether *"the match was acceptable"* and whether to accept the kidney from the Transplant Service. In particular, state whether you considered:

(i) the cold ischaemic time

I would have undoubtedly considered the cold ischaemic time and would have been unlikely to accept the kidney if I believed we were unlikely to be able to perform the transplant within 24 hours of it being donated.

(ii) the *"widely separated arteries on 1 patch"* (Ref: 058-009-030)

Assuming I was aware that there were 2 arteries on a patch, I would certainly have informed the surgeon of this situation and it would have been his decision as to whether he would accept such a kidney. It is not clear to me if the statement "2 arteries widely separated on a patch" was initially communicated or added in Belfast by the Transplant Co-ordinator, Ms E Donaghy, who signed this form.

(d) State whether you discussed any of the factors you have identified in your answer in respect of 'cold ischaemic time' and 'widely separated patch' with anyone, and if so, state when, with whom and explain why. If you did not discuss these factors with anyone, explain why you did not do so.

As I have stated, I would have discussed the potential cold ischaemic time issue and any anatomical information I knew with the transplant surgeon. I would have discussed the time that the UK Transplant Service could deliver the kidney to Belfast so that we remained if possible within the 24 hour cold ischaemic time window.

(e) State, after the tissue cross-match and at the time of your consideration whether or not to confirm the decision to proceed with the transplant, what information you had about the donor kidney and the source of that information, including identifying any relevant document.

I was aware that the kidney had been donated between 1.00 and 2.00am on the morning of the 26th. The information which I had was that provided to me by UK Transplant. The relevant documentation that accompanies the kidney would at that time have been with the kidney at the Belfast City Hospital Renal Unit and would have been scrutinised by the surgeon when he collected the kidney. I did not see the document therefore at that time.

(f) State what factors you considered in deciding whether or not to confirm the decision to proceed with the transplant. In particular, state whether you considered:

(i) the cold ischaemic time

Had the transplant proceeded on the evening of the 26th as initially agreed, I would have accepted the cold ischaemic time. The decision to delay the transplant for several more hours was that of the surgical and anaesthetic team who have stated that they believed operating fresh early in the morning gave the best chance of success of the transplant. I accepted their view and communicated it to Ms Slavin.

(ii) the *"widely separated arteries on 1 patch"* (Ref: 058-009-030)

As regards the issue of the separated arteries on one patch, this was a decision for the surgeon to decide if the arterial structure was unsuitable.

(iii) the implications of not proceeding with the transplant surgery at this time, and if so, what you considered those implications to be

The implications of not proceeding with the transplant surgery at this time would probably have meant that the kidney would not have been used but would have needed to be offered back to UK Transplant in case another centre would be prepared to use the kidney. Adam would have reverted to his normal dialysis regimen.

(g) State, after the tissue cross-match and before you made the decision to confirm the decision to proceed with the transplant, whether you discussed those and other factors with anyone. If so state when, with whom and what you discussed.

These discussions were actively held between the surgeons and anaesthetist and communicated with me. It was not solely my decision to proceed with the transplant.

(h) State when you first knew of:

(i) the cold ischaemic time

I was aware that the kidney had been donated between 1.00 and 2.00am on the 26th when I received the phone call from UK Transplant.

(ii) the *"widely separated arteries on 1 patch"* (Ref: 058-009-030)
and the source of that knowledge

I believe I would also have been informed of the fact that there were two arteries on a patch at that time in the information given to me by telephone and would have communicated that with the transplant surgeon. I have no recollection of the phrase "widely separated".

(i) Describe and explain what Mr. Keane told you in relation to how Adam's surgery would be carried out and any surgical risks to the success of Adam's transplant and/or the risks to Adam. In particular, state if he discussed the following with you, and if so, when he discussed them:

(i) Adam's age and size

I believe that a kidney from a 16 year old for a 20kg boy was considered to be an acceptable size match. A kidney from a child is ideal for a paediatric transplant.

(ii) Adam's multiple previous operations

I would have summarised Adam's previous urological history and his multiple previous operations, some of which had been performed by Mr Brown, and I was therefore pleased that he would be present during the surgery because of his particular knowledge.

(iii) The cold ischaemic time

We certainly discussed the cold ischaemic time and while I would have indicated my preference that the transplant should proceed late on the 26th or during the first hours of the 27th, I accepted the surgeon's view that it was wiser to start the surgery early in the morning.

(iv) The *"widely separated arteries on 1 patch"* (as compared to a single artery)

I do not recollect having any particular discussion about the separated arteries on one patch. Mr Keane would have examined the vessels before proceeding.

(v) The half match of the donor kidney

The half match of the donor kidney would have been discussed, but acceptable for a child who had been on call for over a year.

(vi) The size of the kidney from the 16 year old donor

I do not recollect any discussion of the size of the kidney from the 16 year old between Mr Keane and myself. A decision in relation to the size of the kidney and its transplantation would have been the surgeon's.

(vii) The possibility of not proceeding with the transplant surgery

It is possible that we did discuss not proceeding with the transplant surgery, but decided against this. I would have supported a start within 24 hours of donation.

(j) State whether you believed on 26th/27th November 1995 that: (i) the cold ischaemic time

and/or (ii) the *"widely separated arteries on 1 patch"* (Ref: 058-009-030) increased the risks of Adam's transplant being unsuccessful, and if so, state:

- The reasons why

I did believe that the cold ischaemic time increased the risks of Adam's transplant surgery being unsuccessful in as much as there was likely to be a prolonged period of recovery from acute tubular necrosis and this was widely recognised in the literature. I believe the double arterial supply could have made the vascular surgery more difficult and perhaps prolong the surgery.

- Whether you discussed these 2 factors and your view with any other person, and if so identify that person and state when and where you discussed this.

The issue of the separated arteries on the patch was an issue for the surgeon rather than for me, and I would have accepted his guidance on that, although I do not recollect that there was any discussion that this was a problem.

If you did not believe these factors increased the risks, state the reasons why not.

(k) State whether you discussed with Adam's mother prior to her providing consent to the transplant the implications of:

(i) Proceeding with the transplant surgery in all the circumstances including the cold ischaemic time, the *"widely separated arteries on 1 patch"* and the other factors listed above

I did discuss the delay in the transplant surgery with Ms Slavin and explained to her that it was because the surgeons felt it was wiser to start on such a major operation after they had gained some sleep and were fresh to the task. I do not recollect discussing the 2 arteries on a patch but may have done so.

(ii) Not proceeding with the transplant surgery at that time
(iii) If so, describe what you told her and state when and where you discussed this with her.
(iv) If you did not discuss this, explain why you did not do so.

I am not certain that I discussed the possibility of not proceeding with the transplant with Ms Slavin at that time, and I would probably have explained that the surgeon felt that delaying the start time was the wisest course of action.

(l) Explain how you *"verified that [Mrs Slavin] was willing to allow the transplant operation"*, and what was discussed at this time in terms of:

(i) the risks and disadvantages of the transplant surgery with this donor kidney

In discussion with Mrs Slavin in relation to proceeding with the transplant operation I have already stated that we believed having a successful kidney transplant was Adam's best chance of achieving a normal childhood and we were already aware of the stress caused by his illness and the psychological effect on his development and on his family. I would have indicated the cross match was satisfactory and a kidney from a young person was ideal (see 20 i) (i) above).

(ii) the risks and disadvantages of not pursuing the surgery at this time

The risks and disadvantages of not pursuing surgery at this time was that we might have to wait a considerable time before another reasonably suitable kidney became available.

(m) State whether you inspected the donor kidney on 27th November 1995 prior to the transplant surgery, and if so, state when, where and who else was present. If not, explain why not.

I did not inspect the donor kidney prior to surgery. This is the responsibility of the transplant surgeon. As a physician, I would not be in a position to evaluate whether it was feasible to perform the operation successfully.

(21) Answer to Question 6(a) at p.12:

"Information regarding renal transplantation was given to Adam's mother prior to Adam being put on call on the national database and before his tissue type was analysed. Patients would not be registered on call for a kidney transplant without the express consent of parents. The nature of the transplant process, the need for the tissue typing, for a cross-match if a kidney was offered and the fact that this was major surgery, including the risks of such surgery and of anaesthetic, would have been explained. Ms Strain was always understandably anxious when Adam required further surgery, bearing in mind, the number of times he had been to theatre. I believe she was apprehensive in relation to such major surgery because of previous experience and because she recognised the potential risk to his life. I am satisfied that she weighed up these risks against the potential of a successful transplant giving Adam a normal life. Whilst I cannot now specify the exact dates when discussions took place, Adam's mother had a close relationship with the renal team and discussions about transplantation took place on many occasions. She would have been provided with a Transplant information book, as was usual practice. A copy has previously been provided to the Inquiry."

(a) Specify *"the risks of such surgery and of anaesthetic"* that were explained to Ms. Slavin prior to Adam's transplant surgery and identify who would have explained them to her.

Ms Slavin was aware that every anaesthetic and operation carried a significant risk to small children. She had had the experience of facing that situation many times before. I believe I explained to Ms Slavin that the transplant surgery was a bigger and more complex operation than operations on the bladder which Adam had previously undergone. I would have explained that there was a vascular anastomosis involved and that this type of surgery carried a greater risk of bleeding and complications, particularly in small children. I would have explained to her that the operation was likely to last for four hours and therefore the risk of the anaesthetic might be proportionately greater. I believe that I discussed Ms Slavin's worries and concerns about surgery in relation to Adam on many occasions. I would have expected the transplant surgeon and consultant anaesthetist to also talk to Adam's mother.

(22) Answer to Question 6(b) at p.12:

"I alerted Adam's mother to the offer of a kidney when I had received this information from the UK Transplant Service. I asked her to bring Adam to the ward as she was willing to proceed with the transplant so that we could initiate the appropriate investigations, including a tissue

cross-match. I have not recorded the exact information which I gave to Ms Strain on 26 November 1995. To my recollection I would have informed her that it was an adult kidney which the transplant surgeon planned to use. It is likely I informed her that a paediatric surgeon would also be involved in the surgery who had knowledge of Adam's previous surgery who would therefore be available instantly during the transplantation procedure. I would have explained that we needed to cross-match several units of blood because of the risk of blood loss during surgery so that this could be replaced if necessary. I would have explained the need for the change in his normal overnight feeds so that his stomach was empty at the time he received his anaesthetic and also the plan to give him some intravenous fluids once tube feeds ceased until such time as he got to theatre. I do not remember in what detail I discussed the risk to Adam's life. I believe we both understood there was such a risk and hoped and expected he would come through the procedure successfully. Ms Strain subsequently signed the consent form for us to proceed when we knew the tissue cross-match was satisfactory but understandably was worried about her son undergoing major surgery."

(a) You have not adequately answered the question. State what information you gave Adam's mother about the risks of the transplant surgery and anaesthesia, please include what you explained to her about the source of those risks.

It is difficult to be more explicit as to the content of my conversation with Adam's mother prior to the surgery. I have answered as honestly as I can and as I have said in answer to previous questions, I would probably have explained to her that there is a risk to a child's life from such major surgery but I am unlikely to have given any percentage risk, although I would have considered it to be small, possibly 1-2%. The risks of surgery and anaesthesia are best explained by the specialists in those fields.

(b) Explain why you believed that Adam's mother *"understood there was such a risk [to Adam's life] and hoped and expected he would come through the procedure successfully"*

I have made this statement because I believe this was the understanding between us.

(c) State whether you were aware of the composition of the anaesthetic and surgical teams when you informed Ms. Slavin that *"a paediatric surgeon would also be involved in the surgery who had knowledge of Adam's previous surgery"*.

I knew the consultants who would be involved.

(d) State when you first knew that Mr. Stephen Brown would act as that paediatric surgeon.

I expect that I knew that Mr Brown would be the paediatric surgeon sometime on the evening of the 26th and therefore would probably have been aware when I spoke to Ms Slavin late on that evening that he would be the surgeon involved.

(e) Explain your reasons for not informing Ms. Slavin, prior to surgery, that the second surgeon would be Mr. Brown, including what consideration you gave to her previously expressed concerns over Mr. Brown's involvement in Adam's care.

There was no reason why I would have not informed Ms Slavin that Mr Brown would be the paediatric surgeon involved in assisting Mr Keane during the transplant surgery. I do not remember that I did not inform Ms Slavin of Mr Brown's involvement, and if such an omission did occur, it would certainly not have been intentional.

(f) Explain the reasons why it was necessary that *"a paediatric surgeon would also be involved in the surgery who had knowledge of Adam's previous surgery"*.

My understanding of this arrangement is that the adult transplant surgeons always had an assistant working with them during this type of surgery and that Mr Brown as a senior paediatric surgeon offered his services, and this seemed to me to be very much to the patient's benefit, particularly as he had intimate knowledge of the anatomy of Adam's renal tract following his previous surgery.

(g) State the reasons why you did not inform Ms. Slavin prior to the surgery of the level of surgical experience in carrying out paediatric renal transplants of both Mr. Keane and Mr. Brown.

I would not have necessarily been aware of the exact surgical experience of Mr Keane in carrying out paediatric renal transplants and it would probably not have been my normal practice to discuss such issues with parents. Mr Brown, of course, was only assisting Mr Keane, but was an experienced paediatric urological surgeon. Such close working was recommended in The Tertiary Services for Young People document identified in Question 1(f).

(23) Answer to Question (6)(c) at p. 12:

"The consent form was signed on 27 November 1995. The exact time has not been noted. See 6(b) above."

(a) You have not adequately answered the question. Please state what information regarding consent was given to Adam's mother.

The consent form was probably signed between midnight and 2.00am. I have no clear memory of the detailed information which I gave to Ms Slavin at that time, but it would have probably included the age of the donor, the level of the tissue match, the fact that the cross-match was favourable, an estimate of how likely the transplant was to be successful (usually around 90%), the risks of this type of surgery, including risks of vascular surgery, the need for a urinary catheter to be placed, the need for a central line, and some details of the proposed anaesthesia and epidural analgesia. I refer to answers in Question 21 & Question 22 above.

(b) Please explain the reasons why you, and not Mr. Keane (the consultant transplant surgeon) or Mr. Brown (the consultant paediatric surgeon assisting him), gained consent for the renal transplant from Adam's mother.

In 1995, it was not uncommon for initial consent to be obtained by someone other than the surgeon carrying out the procedure. Generally, the surgeon and anaesthetist would speak with the parents immediately prior to surgery to confirm that they understood the detail. Current procedures at RBHSC require the person carrying out an operation to obtain consent and list any possible complications and risks. Parents are also asked to sign that these have been explained.

(24) Answer to Question 7(d) at p.13:

"In relation to laboratory tests, blood samples would have been obtained by a doctor and taken to the appropriate laboratory, along with the request forms, by a porter. Results of the tests would be phoned to the ward and recorded by the doctor who received them in the patient's notes."

(a) State the turn-around time for obtaining blood test results from the laboratory 'after hours'.

For an urgent request to the portering and laboratory service, I would estimate that the turnaround time would be under one hour.

(25) Answer to Question 7(e) at p.13:

"I provided a copy of the renal transplantation in small children protocol for reference by the junior doctors involved, Dr Cartmill and Dr O'Neill, and requested that they carry out the appropriate investigations. Subsequently I checked that these had been performed."

(a) Explain for whose attention and/or guidance the *"renal transplantation in small children protocol"* of 1990 was compiled and provided

A copy of the renal transplantation protocol was kept with the notes of any child being considered for transplantation so that it would be available to all nursing and medical staff for consultation. This includes consultants.

(b) Identify who had the responsibility to ensure that the *"renal transplantation in small children protocol"* of 1990 was complied with

It would have been the responsibility of the Consultant Nephrologist to ensure that the renal transplantation protocol was followed.

(c) State when you *"provided a copy of the renal transplantation in small children protocol for reference by the junior doctors involved, Dr Cartmill and Dr O'Neill"*.

When Adam was admitted on 26th November for a renal transplant, a copy of the protocol was placed with his notes for consultation by all involved, including Dr Cartmill and Dr O'Neill.

(d) Specify what *"the appropriate investigations"* were in November 1995.

Appropriate investigations in 1995 are those listed in the transplantation patient protocol previously provided to the Inquiry. These include: samples of blood taken for tissue typing, for grouping and cross matching 4 units of blood, for estimating haemoglobin, full blood picture white cell and platelet count, blood to estimate urea and electrolyte levels and blood to check for virology status. Urine and peritoneal dialysis fluid was collected for culture, and a chest x-ray performed.

(e) State how and when you checked that *"the appropriate investigations"* required by the renal transplant protocol had been carried out by Drs. Cartmill and O'Neill.

I believe I checked these investigations had been carried out in the early hours of the morning of the 27th November before going home.

(f) Identify any note or other evidence of such a check being made.

I have noted in the clinical notes in the early hours of the 27th November, that the appropriate checks had been made (Ref: 058-035-133).

(g) Explain the extent to which the *"the renal transplantation in small children protocol "*in respect of Adam's renal transplant was adhered to by the clinicians and nurses involved, providing instances of any non-compliance and explain:

(i) how they arose
(ii) what was done about them

I believe that the appropriate procedures were carried out according to page 1 of the admission protocol in the renal transplant guidance, although a record of urine output would have been impossible.

(26) Answer to Question 7(g) at p. 14:

"Adam's weight is recorded on document 057-012-016 as 20.2kg in the weight chart prior to overnight feeds..."

(a) State whether Adam's weight was taken before and after the dialysis on 26th/27th November 1995, and if so, identify the relevant record. If Adam's weight was not measured at those times, explain the reasons why not.

I have been unable to identify a dialysis record sheet which would have included a pre and post-dialysis weight if available.

(27) Answer to Question 7(h) at p. 14:

"The results of Adam's blood tests are recorded in his notes on 26 November 1995 at 11.00pm... I have made a note on the early hours of 27 November 1995... at the time when the cross-match result became available. On that note I have said his electrolytes were satisfactory but should be repeated first thing in the morning. I would have been aware of the serum sodium result at that time."

(a) Explain fully the reasons why you directed that Adam's electrolytes *"should be repeated first thing in the morning"* and the purpose of the repeat electrolyte test.

Adam's surgery had been delayed and I therefore thought it was wise to have an estimate of his electrolytes immediately prior to surgery rather than from late the previous evening. Furthermore, Adam was having a short period of dialysis and some tube and IV fluids overnight and again I thought it would be wise to check that his electrolytes had remained in the normal range. His normal overnight regimen was being adapted. It was therefore important to be sure this had not caused any change in his electrolyte status.

(28) Answer to Question 8(a) at p.14:

"The arrangements for securing an operating theatre for a transplant involved contacting the senior nurse in theatre and alerting her to the fact that a possible renal transplant might occur

in several hours, and from whom the Consultant Anaesthetist would be identified. The Anaesthetist was contacted to alert him again to the possibility of a renal transplant and confirm that he was willing to undertake an anaesthetic for that surgery. On this occasion it was Dr Bob Taylor. From the surgeon on call list for renal transplants held in the Renal Unit in the BCH, the transplant surgeon was identified. On this occasion Mr Patrick Keane confirmed that he was available and willing to carry out a paediatric transplant. Ideally, the presence of a senior paediatric surgeon who could be present and assist with the transplant is required. On this occasion, Mr Stephen Brown agreed to assist Mr Keane. I cannot say exactly what time these arrangements were finalised on the evening of 26 November 1995. I had no part in involving Dr Terence Montague."

(a) You have not adequately answered the question. Please identify the persons that <u>you</u> contacted, including whether <u>you</u> contacted Dr. Robert Taylor, Mr. Patrick Keane and Mr. Stephen Brown. If you did not contact Dr. Taylor and Messrs. Keane and Brown, identify the person who did contact each of those persons.

I personally contacted Dr Taylor, Mr Keane and Mr Brown.

(b) Identify the *"senior nurse in theatre"* who was contacted.

I do not know the name of the senior nurse in theatre on that occasion.

(c) Explain why it was necessary to ask Dr. Taylor whether *"he was willing to undertake an anaesthetic for that [renal transplant] surgery".*

In contacting the consultant anaesthetist on call, it was important to know that he would be completely free to be the anaesthetist for the transplant surgery. If for example, there was some other major surgery required that evening as a result of some major trauma, then a second anaesthetist might have been needed to become involved. There is perhaps also an issue whereby consultant anaesthetists have specific areas of expertise which might also influence the decision as to who the consultant anaesthetist for a renal transplant might be. I had no concerns in relation to Dr Taylor's expertise.

(d) State the number and identity of the transplant surgeons who were on *"the surgeon on call list for renal transplants held in the Renal Unit in the BCH"* for any paediatric transplant to take place on the morning of 27th November 1995.

I cannot answer this question except to say there was one surgeon listed for transplants each day.

(e) Explain the system, if any, in operation in November 1995 at the RBHSC for obtaining an appropriately trained surgeon capable of performing a paediatric renal transplant to carry out such a transplant, in particular explain:

(i) whether the system included having a transplant surgeon on-call who was appropriately trained and capable of performing a paediatric renal transplant

(ii) how, if the system did not include having a transplant surgeon on-call who was appropriately trained and capable of performing a paediatric renal transplant, an appropriate transplant surgeon was obtained once a kidney became available and who was responsible for obtaining such a surgeon

The system in operation for obtaining a transplant surgeon if there was an offer of a paediatric renal transplant, was that the transplant surgeon on call was contacted and it was their decision as to whether they felt they were appropriately trained and capable of carrying out the procedure. If the transplant surgeon on call judged that a more experienced surgeon should undertake the procedure, they would have made that arrangement or advised that the transplant should not proceed.

(f) Explain the reasons why confirmation was sought from Mr. Keane that he was *"willing to carry out a paediatric [renal] transplant."*

It was for the reason explained in (e) above, that I would have sought confirmation that Mr Keane was willing to carry out the paediatric renal transplant.

(g) Explain what you mean by *"senior"* when you refer to *"a senior paediatric surgeon"*.

By "senior paediatric surgeon" I mean a consultant paediatric surgeon, although on some occasions, an experienced senior registrar might have assisted.

(h) Explain the reasons why *"the presence of a ...paediatric surgeon"* who is *"senior"* *"is required"*.

The reason to have a senior paediatric surgeon assisting is to have the combined expertise of both a consultant transplant surgeon and a consultant paediatric surgeon operating together in the best interest of the patient.

(29) Answer to Question 8(b) at p.15:

"The anaesthetist on call is informed, the surgeon on call is informed and a surgical assistant is identified. This team then take forward arrangements for the surgical aspects of the transplant."

(a) Explain what *"arrangements for the surgical aspects of [Adam's] transplant"* you understood would be *"taken forward"* by that *"team"*

Once the nephrologist has identified the consultant anaesthetist and consultant surgeon leading on the transplant, it is for them to take forward the more detailed arrangements. For example, identifying the theatre that would be used, the ideal start time, and briefing the nurse in charge in theatre. I would expect that the surgeon and the anaesthetist would meet with the parents, examine the child, and that the surgeon would confirm that the appropriate instruments were available, and after examination, assure himself that the kidney was suitable for transplant into that child.

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

"I do not have a definite memory of the exact time when I had telephone discussions with Dr Bob Taylor, Consultant Anaesthetist, and Mr Patrick Keane, Consultant Surgeon on the late evening and early morning of 26 and 27 December [sic]. Discussions with Dr Taylor would have been in relation to Adam's previous medical history and his diagnosis of obstructive uropathy and polyuric renal failure. His previous urological history, his multiple previous anaesthetics and operations and the fact that he was fed by gastrostomy with a high calorie Nutrison feed which was required to be delivered in high volumes of 2.1 litres daily. I would have informed Dr

Taylor of Adam's current medical condition, his size, level of nutrition and difficulties with venous access. This discussion led to the development of a plan for his fluid management prior to the surgery, essentially changing from a high density Nutrison feed to clear fluids that would empty from his stomach more rapidly, and the need to discontinue all feeds two hours before surgery (see question 10 a). I would have informed Dr Taylor of his current electrolyte and urea status and agreed the need for a further blood sample immediately before surgery if the transplant operation was delayed overnight.

(a) Describe and explain what you told Dr. Taylor (or believe that you would have told him if you cannot actually remember exactly what you said) in relation to Adam's:

(i) diagnosis of *"obstructive uropathy and polyuric failure"*, including in both cases the implications of those diagnoses for the formulation of a fluid management plan for Adam's transplant surgery

I believe I would have told Dr Taylor that, despite the fact that Adam had chronic renal failure and was maintained on dialysis, that because of his initial diagnosis of obstructive uropathy he had a polyuric type of renal failure. As I have stated in an earlier answer to the question, Adam required to have 2.1 litres of fluid daily, so that he could build a calculation of his basic fluid requirements during the transplant surgery.

(ii) *"previous urological history"*

I would probably have given a brief summary of the previous urological surgery, including re-implantation of his ureters in infancy which had required subsequent revision so that one ureter cross-drained to the contra-lateral side so that he would be aware that the transplant surgery might be complicated by the previous bladder operations.

(iii) *"multiple previous anaesthetics and operations"*

I would have reminded Dr Taylor of the multiple previous operations which Adam had had, as he may have wished to review the previous anaesthetic records, although I was probably aware that Dr Taylor had previously anaesthetised Adam.

(iv) *"high calorie Nutrison feed which was required to be delivered in high volumes of 2.1 litres daily"* and was fed by a *"gastrostomy bag"*

The high calorie Nutrison feed was discussed in terms of how much oral feed we could give Adam and when it should be discontinued prior to surgery. It is known that Nutrison is slow to empty from the stomach and this would have influenced the decision to change to clear fluids overnight to ensure that the stomach was empty prior to administering an anaesthetic. I may have also indicated that the sodium content of Nutrison is similar to that of 1/5 normal saline. I would emphasise that I do not exactly remember the details of the discussion between myself and Dr Taylor and that these comments are as you have requested what 'I believe I would have told him'.

(b) Describe and explain in relation to each of the factors above:

(i) what you told Dr. Taylor (or believe that you would have told him if you cannot actually remember exactly what you said) about their significance for any fluid

management plan for Adam's transplant surgery

(ii) their significance for any fluid management plan for Adam's transplant surgery

I have answered this question in (a) above.

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

I believe that Dr Taylor understood that Adam required 2.1 litres of fluid each day and that he had a polyuric type of renal failure, probably passing 1200mls of fluid per day. I believe that Dr Taylor made plans to take this into account when managing his fluid balance during surgery.

(d) Describe and explain what you told Mr. Keane (or believe that you would have told him if you cannot actually remember exactly what you said) in relation to Adam's:

(i) diagnosis of *"obstructive uropathy and polyuric failure"*, including in both cases the implications of those diagnoses for Adam's transplant surgery

I believe that I would have told Mr Keane that Adam had been born with an obstructive uropathy and a degree of renal dysplasia. I would have explained that surgery to re-implant his ureters had only been partially successful and required revision so that one of Adam's ureters was cross-connected to the other rather than to his bladder. I would also have explained to him that despite the fact that Adam was maintained on peritoneal dialysis he still had a significant urine output.

(ii) *"previous urological history"*

I would have given a brief summary of his previous urological surgery as in (d)(i) above.

(iii) *"multiple previous anaesthetics and operations"*

I would have explained that Adam had had many previous operations, including those recently to produce a gastrostomy and to place peritoneal dialysis cannulas.

(e) In relation to *"changing from a high density Nutrison feed to clear fluids"*, state precisely what you meant by *"clear fluids"* and describe their content.

I have stated that the clear fluids to be given overnight was Dioralyte (Clinical notes Ref: 058-035-133). Dioralyte contains 60mmol of sodium per litre, 20mmol of potassium per litre, and glucose 60mmol per litre when reconstituted.

(f) Explain why you considered that there was a *"need for a further blood sample immediately before surgery if the transplant operation was delayed overnight"*

I believed it was important to have a further blood sample for electrolytes before surgery as the previous sample had been taken before midnight on the 26th November. Overnight Adam would be receiving oral and intravenous fluids and a short spell of peritoneal dialysis and I thought it was important to be sure that his serum electrolytes remained in the normal range since his normal overnight regimen had been adapted.

(g) State your role in ensuring that the *"plan then agreed with the anaesthetic team was that a blood sample for electrolyte and urea estimation be sent to the laboratory once IV access was established in theatre and the fluid deficit be corrected intravenously."* [Ref: WS/002/02 p. 20, Question (11)(i)] was followed prior to your departure from theatre at approximately 09.00.

Having agreed with Dr Taylor that a blood sample for electrolyte and urea estimation would be sent to the laboratory at the commencement of surgery and anaesthesia, I left this as his responsibility.

(h) State whether you were involved in the *"clinical judgment"* [Ref: 011-015-111] not to test Adam's electrolytes once the anaesthetic was administered to Adam, and if so, explain the basis of that judgment. If not, identify the person(s) who made that clinical judgment.

I was not involved in the clinical judgment not to test Adam's electrolytes once the anaesthetic was administered. This was contrary to my request and I presume was made by Dr Taylor.

(i) State whether, between the induction of anaesthesia and your departure from theatre at approximately 09.00 on 27th November 1995, you:

(i) asked for Adam's electrolytes to be tested in accordance with the *"plan"*

At the time I left theatre, I was not aware that a sample had not been sent for electrolyte estimation at the laboratory. I had asked for the electrolytes to be checked when intravenous access had been established under anaesthesia.

(ii) inquired after the results of electrolyte tests

I did not enquire after the results of the electrolytes and presumed that Dr Taylor was happy with the results or he would have raised any concerns with me.

(iii) commented on the departure from the *"plan"* to test Adam's electrolytes

I was not informed that the sample had not been sent.

If you did not do so, please explain your reasons in each case

(j) State whether you were available between the induction of anaesthesia and your departure from theatre at approximately 09.00 on 27th November 1995 to obtain a blood sample for analysis or to arrange for a blood sample to be taken to the laboratory and/or to the blood gas analyser immediately for analysis. If so, state at what time or at what stage during surgery you were so available. If you were not available to do so, then explain why not.

I want to make it clear that I was only available to the theatre team for advice. As a physician, I had no role taking blood samples or analysing them as the patient was now under the care of the anaesthetic and surgical team.

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

My discussions with Mr Keane would have been to explain to him the nature of Adam's previous surgery, including the current anatomy of his urinary tract with two ureters draining by a single lower ureter into his bladder and the fact that he had had major urological surgery before. I would have informed him of the situation with a polyuric renal failure, the nature of the tissue type match and any knowledge I had of the anatomy of the donor kidney from my conversations with the UK Transplant Service. Discussions with Mr Keane also would have involved the choice of time for taking Adam to theatre and arranging for Mr Keane to have a Consultant Paediatric Surgeon to assist him during the operation who had a substantial knowledge of Adam's background surgery and complexity."

(a) State the role and contribution of *"a Consultant Paediatric Surgeon to assist [Mr Keane] during the operation who had a substantial knowledge of Adam's background surgery and complexity."*

I would suggest that Mr Brown is better placed to answer this question than myself, but my perception would be that his experience in paediatric surgery and urology would be extremely useful. Furthermore, Mr Brown had operated on Adam's bladder and ureters initially and therefore had detailed knowledge of the relevant anatomy.

(b) Explain the process by which Mr. Brown came to act as Consultant Paediatric Surgeon to assist Mr. Keane, including:

(i) whether you discussed with Mr. Keane Consultant Paediatric Surgeons who might satisfy the criteria of having *"a substantial knowledge of Adam's background surgery and complexity"*

It is likely that I did discuss with Mr Keane the availability of a consultant paediatric surgeon. I believe Mr Brown may have volunteered to assist when he heard there was a potential transplant for Adam.

(ii) whether Mr. Brown was specifically discussed

I cannot be sure that I specifically discussed Mr Brown with him or his substantial knowledge of Adam's background surgery and complexity.

(iii) whether the concerns that Adam's mother had about Mr. Brown were raised

I cannot remember if I was aware that Adam's mother had concerns about Mr Brown communicated to me in relation to the transplant surgery.

(c) Explain the knowledge about Adam that Mr. Brown was thought to have which warranted his inclusion on the surgical team for the renal transplant.

My belief is that Mr Brown became aware that there was an offer of a kidney for Adam Strain. Mr Brown had been involved in his early urological surgery and had extensive experience of paediatric urological surgery and I believe he offered to assist Mr Keane.

(d) State:

(i) when you had *"conversations with the UK Transplant Service"* and what was

discussed

I believe I only had the one conversation with the UK Transplant Service on the afternoon of 26th November when they would have informed me that a kidney, which had a reasonable tissue match, was available for Adam Strain. I would have been informed of the cause of death of the donor, the time at which the kidney had been donated, the blood group and tissue type of the donor, any significant medical history, and any significant anatomical detail of the donated kidney.

(ii) the knowledge that you *"had of the anatomy of the donor kidney from [your] conversations with the UK Transplant Service"* which you passed on to Mr. Keane and when you passed that information to him.

It would have been normal practice for the UK Transplant Service to inform me that there were two arteries on a patch as was the case with this kidney. However, I have no recollection that they said the two arteries were "widely separated". Having been given such information, I would have undoubtedly passed that information onto Mr Keane when I was asking him if he was available to perform a paediatric transplant. The information would also have been included in documentation provided to Mr Keane by the UK Transplant Service when the kidney arrived in the Belfast City Hospital (Ref: 058-009-030).

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

"I was informed by phone that venous access was no longer available to provide intravenous fluids after returning home at 2.00am on 27 November 1995. When repeated attempts failed, the Anaesthetic Senior Registrar (Dr Terence Montague) was contacted for assistance. Adam was very distressed and after consultation with Dr Taylor, the Consultant Anaesthetist, they agreed to make no further attempts (093-037 Witness Statement). I advised an increase of the fluids through his gastrostomy tube to compensate for this. I advised 200mls per hour was the maximum we should deliver in order to avoid vomiting from over-filling Adam's stomach. It had been agreed with the anaesthetist that no fluid should be given through his gastrostomy [tube] for 2 hours before going to theatre. I would have communicated this to the ward nursing staff."

(a) State when you *"advised an increase of the fluids through his gastrostomy [tube] to compensate for this."*

I would have advised an increase in the fluid through Adam's gastrostomy tube at the time when I was informed that venous access was not possible. The fluid balance sheet indicates that this change was made at 2.00am.

(33) Answer to Question 9(e) at p.16:

"The decision to postpone Adam's surgery from the time when we knew that his cross-match was suitable to early morning on 27 November 1995 was agreed between the surgical and anaesthetic team. I understand that the rationale for an early morning start was so that surgeons, anaesthetists and nursing staff were fresh starting a day's work rather than finishing a shift. The surgical and anaesthetic consultants believed that this was a safer option for the patient. I do not know why there was a change from 6.00am to 7.00am."

(a) State when the new shift started on 27th November 1995 for:

(i) Nurses
(ii) Anaesthetists
(iii) Surgeons.

I believe nursing shifts change at 8.00am. I do not know the nature of the shift system in relation to anaesthetists and surgeons at that time.

(34) Answer to Question 9(f) at p. 16:

"...It is now clear to me that the kidney was re moved at 01:42 on 26 November 1995 as recorded on the Kidney Donor Information Form.... In my previous statement I have suggested 16 hours. I had not remembered this detail and assumed the kidney had been donated at 1.42pm."

(a) State the date and time when you first knew that the kidney had been donated on 26th November 1995 at 1.42am.

I believe I knew on 26th November when the UK Transplant Service first contacted me that the kidney had been donated at 1.42am. I believe my error in regards to the time was in the statement, not at the time of surgery.

(b) State whether you discussed the cold ischaemic time of the kidney, if so, state when, where, with whom and the outcome of the discussion.

I would have discussed the cold ischaemic time of the kidney with the transplant surgeon during our discussions on 26th November.

(c) If you had known the actual cold ischaemic time of 28 hours and not 16 hours, what difference, if any, would it have made to your actions and state the reasons why. If this knowledge would have made no difference, state the reasons why not.

I believe I was concerned about the long cold ischaemic time on 27th November, but accepted the advice of the surgical and anaesthetic consultants that it was best from the patient's point of view to delay the surgery until early morning.

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

"As far as I remember, I had discussions with the anaesthetic team at the time of Adam's transfer to theatre to include, reviewing his evening electrolyte results, the fluids he had received overnight and the fact that his venous line had tissued so that he had not received some of the intravenous fluids as planned and that it had not been possible to obtain a blood sample so a pre-theatre electrolyte measurement was still outstanding."

(a) Identify the members of the anaesthetic team with whom you had discussions *"at the time of Adam's transfer to theatre"*.

I discussed the situation relating to Adam's overnight fluids with Dr Taylor.

(b) Describe in as much detail as possible the *"discussions with the anaesthetic team at the*

time of Adam's transfer to theatre" and whether this resulted in any changes to Adam's fluid management plan in theatre. If so, state why and describe the changes, and if not, explain why not.

I wish to emphasise again that I do not remember details and can only state what I believe I would have discussed with Dr Taylor at the time of Adam's transfer to theatre. I believe that we would have discussed that there was a deficit in the amount of fluid which had been planned for Adam compared to what he actually received. I believe that Dr Taylor then planned to make up this deficit during the first one or two hours of the surgical procedure.

(c) State whether you or any member of the nephrology team had directed any ward nurse/s to note details relating to Adam's fluid balance whilst being dialysed including the volume of urine produced by Adam, Adam's weight pre and post dialysis, and details of all fluid administered to or taken in by Adam during his dialysis on 26th/27th November 1995, and if so, identify the person who gave that direction, and state whether this direction was followed and if so, state by which nurse and where this information is recorded. If you did not give this direction, explain why not.

I would have directed that Adam's fluid balance would have been carefully recorded in terms of both input and output on a fluid balance chart during the 26th and 27th November. This would be standard nursing practice. His urine output would therefore have been measured if possible and his weight, both pre and post-dialysis, recorded. I do not know the identity after this time of the nurse responsible for looking after Adam that evening.

(d) At *"the time of Adam's transfer to theatre"* state whether you were aware of information relating to Adam's fluid balance whilst being dialysed including the volume of urine produced by Adam, Adam's weight pre and post dialysis, and details of all fluid administered to or taken in by Adam during his dialysis on 26th/27th November 1995, and if so, state whether you provided this information to any member of the anaesthetic and surgical teams, identifying that member and state when you provided that information and what information you provided to them. If you were not aware of that information, state the reasons why not.

While there is no clinical note in relation to post-dialysis assessment, I would have been aware that Adam had received some 970mls of fluid overnight and there undoubtedly was discussion between myself and Dr Taylor that he was some 500mls in deficit, since in the normal evening Adam would have received 1500mls of tube feed. I would have checked on Adam's dialysis overnight, but unfortunately I am unable to locate a dialysis record sheet in the clinical notes and cannot substantiate this.

(e) State whether post dialysis Adam was clinically examined prior to the administration of the anaesthetic, and if so, state when, where, by whom, the findings of the examination and the record thereof. If not, state the reasons why not.

I do not think there is any record of Adam being clinically examined prior to the administration of the anaesthetic, but I believe this would have been normal practice by the consultant anaesthetist. There is a preoperative assessment note on the Anaesthetic record with an ASA classification grade3.

(36) Answer to Question 10(d) at p.18:

"The estimate of Adam's urine output was based on the fact that he received 2.1 litres daily. Insensible loss was based on the formula 300mls/m2/day. The ultrafiltration loss from his dialysis was around 400mls daily. Therefore, if he received 2.1 litres (2100mls) and lost 700mls by these means, one would estimate that he passed perhaps 1400mls of urine. Also, as on occasions he might vomit or not receive the full 2.1 litres, we estimated a range of urine output between 1200-1500mls."

(a) State when Adam's daily urine output was last actually measured, and identify the record of that measurement in Adam's notes.

I am unable to identify an accurate measure of Adam's urine output, except for the record in the intensive care unit on 27th November 1995, when he passed 1363mls of urine in a 21 hour period. While it is possible there was some output from the transplanted kidney, these volumes are nevertheless, consistent with our estimate of urine output from his native kidney of between 1200-1500mls.

(b) State Adam's surface area on 26th/27th November 1995 and how you calculated it.

Adam's surface area was calculated as 0.75m² from a nomogram based on a weight of 20.2kg and a height of 102cm recorded on the day of his admission.

(c) Explain the basis of the formula you used to calculate insensible loss.

The insensible loss formula was based on recommendations in the Paediatric Vade Mecum, page 207, published in 1989 by Edward Arnold and edited by J Insley. Advice on insensible loss estimated in this way varies from 3 to 400mls/m².

(37) Answer to Question 11(e) at p.19:

"My understanding was that once Dr Taylor established IV access in theatre, a blood sample for electrolytes and urea would be drawn and the fluid deficit corrected by IV infusion. Subsequently, a maintenance infusion at 85mls/hr would be required to equate with the normal daily intake of 2.1L."

(a) Explain the basis of your understanding that "*once Dr. Taylor established IV access in theatre, a blood sample for electrolytes and urea would be drawn*".

The basis for my belief that the blood sample for electrolytes and urea would be sent from theatre was based on my conversations with Dr Taylor and the instruction that such a sample was required prior to theatre, although subsequently venous access was lost.

(b) State the amount of "*the fluid deficit*" which you believed at the time was to be "*corrected by IV infusion*" during Adam's surgery.

The amount of fluid deficit which I believe was required to be corrected by IV infusion during Adam's surgery was approximately 500mls. This is based on the fact that he normally received 1500mls of gastrostomy feeds overnight, but on the night in question, he only received 970mls.

(c) State the period of time over which you would have expected the fluid deficit to be "*corrected by IV infusion*".

The period of time over which I would have expected the fluid deficit to be corrected by IV infusion would probably have been of the order of 1 to 2 hours.

(38) Answer to Question 11(e) at p.20:

"Addressing the deficit over 2 hours would seem to be reasonable as it generally takes this length of time at least before vascular clamps are released to initiate perfusion of the kidney. Rapid intravenous fluid corrects circulating blood volume almost immediately. The same volume given orally would be much slower in producing this effect."

(a) You state *"addressing the deficit over 2 hours would seem to be reasonable"*.

(i) Quantify the deficit to which you refer and explain your reasoning

The quantity of the deficit is 500mls as explained in 37 (b) above.

(ii) Explain the basis for your view that *"addressing the deficit over 2 hours would seem to be reasonable"*

As I have stated, at the time when vascular clamps are released, it is important that there is a good circulating volume at this point so that the new kidney is well perfused. This is usually monitored by addressing the level of the CVP and Dr Taylor was carrying out such a monitor.

(iii) State if you discussed your view with anyone. If so, state when, with whom and the result of your discussions.

I do not believe I discussed the speed with which the deficit should be made up with Dr Taylor or anyone else.

(b) Describe and explain what at that time you regarded as an appropriate rate of administration to correct *"the deficit"*. Please state what your view would be now, if any different from that in 1995

The 500ml deficit could be given in 1-2 hours, depending on the CVP monitor measure of blood volume. I do not think this differs from my view in 1995.

(c) State what rate of IV administration of N/5 (0.18%) saline in 4% dextrose you understood would be employed by the anaesthetic team during Adam's transplant surgery to *"address ... the deficit"*, and in particular during the first 2 hours of surgery. Please provide the basis of your understanding.

I was not aware of the nature of the fluid and the rate of administration to the best of my knowledge.

(d) Describe what you understand was the actual period over which that *"deficit"* was addressed and comment upon it including on the 500mls of N/5 (0.18%) saline in 4% dextrose infused over the first half hour of anaesthesia [Ref: 058-003-005]. Also provide the basis for your understanding.

I believe the deficit was included in the 500mls of N/5 saline in dextrose infused during the first half hour of anaesthesia from statements provided by Dr Taylor to the Coroner.

(e) Describe the volume and type of fluid that you understand was actually administered to Adam and its rate of administration over the first 2 hours of anaesthesia, and comment upon it. Also provide the basis for your understanding.

On perusing the anaesthetic record (Ref: 058-003-004), my understanding is that at least 1000mls N/5 saline in dextrose was delivered over the initial 2 hours of anaesthesia. It also appears that 500mls of Hartman's solution was commenced during the second hour and 400mls HPPF was administered in the second hour. If this is correct, although Adam may have been 500mls in deficit prior to the induction of anaesthesia, this seems like an excessive amount of fluid and equates almost to his normal full daily oral intake (2.1 litres). I accept there may have been other losses of blood during this period and there is a need for volume expansion prior to releasing the vascular clamps so that there is adequate fluid in the circulation to fill the transplanted kidney.

The anaesthetic record indicates that a total of 3500mls of intravenous fluids were administered before the end of the operation. If we accept that 60mls per hour of urine was Adam's normal output, this would be approximately 300mls during surgery. There is a nurse recorded blood loss of 911mls (058-007-021) and we believed there was a fluid deficit of some 500mls when he first went to theatre. The total fluid losses would appear to be of the order of 300mls for urine, 500mls for fluid deficit and 1200mls of blood loss (Anaesthetic record 058-003-005), giving him an estimated total requirement of 2000mls, suggesting Adam may have received 1500mls of excess fluid, .In this context the 1500mls of N/5 saline in dextrose may have resulted in dilutional hyponatraemia.

(f) Explain the rate of administration to which you refer as *"Rapid intravenous fluid"*.

Rapid intravenous fluid administration is utilised in situations of shock or severe dehydration. In such situations 20 mls/Kg of N saline might be administered over 15 minutes .

(g) Explain the basis for that statement and the mechanism by which *"Rapid intravenous fluid corrects circulating blood volume almost immediately"*.

Volumes of 10-20mls per kilogram given rapidly over 15 minutes create an expansion in circulating volume. The basis for this statement is if rapid bolus of fluid is given directly into circulation it adds that volume to the circulating blood quickly, although it may redistribute to extra vascular body space.

(39) Answer to Question 11(g) at p.20:

"There was an instruction to repeat Adam's blood chemistry before going to theatre. This was because there was an alteration in his normal overnight fluid management and I wanted to be sure this had not adversely affected his electrolyte status prior to surgery."

(a) State how *"an alteration in [Adam's] normal overnight fluid management"* could have *"adversely affected his electrolyte status prior to surgery."*

There are several mechanisms by which Adam's electrolytes might have been adversely

affected by the change in his overnight fluid management. For example, if there was a significant deficit in the amount of fluid which he received compared to normal, if the fluid that was administered had a significant difference in sodium concentration, or if the dialysis regimen differed from a normal night. A repeat urea and electrolyte sample prior to surgery on induction of anaesthesia was therefore important.

(40) Answer to Question 11(i) at p.20:

"The plan then agreed with the anaesthetic team was that a blood sample for electrolyte and urea estimation be sent to the laboratory once IV access was established in theatre and the fluid deficit be corrected intravenously. I was not made aware that a sample was not sent or of the serum sodium of 123mmol/L on the gas machine, which if accurate, indicated a significant fall."

(a) State the names and job titles of the members of *"the anaesthetic team"* with whom you agreed the plan *"that a blood sample for electrolyte and urea estimation be sent to the laboratory once IV access was established in theatre and the fluid deficit be corrected intravenously."*

I agreed the plan in relation to sending a blood sample from theatre with Dr Taylor.

(b) State what you would have done and the reasons why, if you had been *"made aware... of the serum sodium of 123mmol/L on the gas machine"*, including whether you would have sought a reassessment of the IV fluid requirement. If you would have sought a reassessment of the IV fluid requirement, state what you would have assessed Adam's IV fluid requirement to be.

If I had been made aware of a serum sodium concentration of 123mmol per litre on the gas machine, I would have wanted to have this reading confirmed from the biochemistry laboratory. While waiting for the result of this laboratory test, I would probably have reassessed the IV fluid requirement and treatment to date with Dr Taylor. A reading as low as 123 would have made me concerned that Adam had received an excessive amount of intravenous fluid. The sodium of 123 on the blood gas analyser is recorded at 9.32am. My retrospective estimate of Adam's fluid requirement up to that time would have included approximately 500mls (overnight intake deficit), perhaps 200mls for normal fluid requirement (2100mls over 24 hours averages to 85mls/hour), and an amount for blood loss – perhaps 300mls. Thus a figure of 1 litre of fluid seems a reasonable estimate from this distance. At that point, Adam had probably been given 2 litres (058-003-005) of IV fluid. If the sodium level was confirmed and the fluid input is correct, I would have recommended an immediate cut back in his fluid intake and considered the administration of 20% mannitol or a strong (2.7%) saline Sol^{n}.

(41) Answer to Question 13(b) at p.22:

"I did not have a role in the plan for Adam's fluid management during the course of the surgery, other than to indicate that he was in fluid deficit at the start. Once his care was handed over to the anaesthetic and surgical team and they were aware of the situation as regards fluid balance and the need for further electrolyte estimation, I was not directly involved in fluid management decisions. I cannot be certain that I met with Adam's mother prior to the surgery that morning or what I discussed with her. It would have been my habit to talk to parents at this stage and inform them that I would be in contact with the procedures in theatre and update them on how

the surgery was progressing over the next number of hours."

(a) State the volume of the *"fluid deficit at the start"* of surgery which you indicated, and identify to whom you gave this indication.

I believe the fluid deficit at the start of surgery was of the order of 500mls, bearing in mind that Adam generally had 1500mls of gastric feed overnight, but had only received a total of 970mls of fluid on the night in question.

(b) State when the care of Adam was *"handed over to the anaesthetic and surgical team"*.

The care of Adam was handed over to the anaesthetic and surgical team once he left the medical ward on the morning of the 27th November.

(c) Identify to whom you refer as being aware of:

(i) *"the situation as regards fluid balance"* and
(ii) *"the need for further electrolyte estimation"*

I believe that the individual to whom I refer as being aware of the situation as regards fluid balance and the need for a further electrolyte estimation, was the consultant anaesthetist Dr Taylor.

(d) Explain how *"they"* became aware of (i) and (ii) above.

I believe he became aware of this situation both in consultation with his registrar overnight and following discussion with myself. The anaesthetic registrar overnight had consulted Dr Taylor in relation to the inability to establish an intravenous line.

(e) Describe *"the situation as regards fluid balance"* of which you state *"they were aware"*.

The fluid balance situation refers to the approximate 500mls deficit in oral fluids given overnight compared to a normal night.

(42) Answer to Question 14(a) at p.22:

"While it was not normal practice for a nephrologist to be present during a renal transplant, since we are physicians rather than surgeons or anaesthetists, it was my habit to observe the procedure intermittently and always be present close to the theatre for consultation should information be required by the transplant team. I would have been changed into theatre scrubs but would not have been gowned as an observer. Up until 9.00am at any time when I was in theatre, there were no problems with Adam about which I was made aware or consulted. When I handed over to my colleague Dr O'Connor and left theatre, I spoke to Ms Strain to let her know the epidural was in place and that things were proceeding slowly with no problems at that stage."

(a) State whether you were aware of the CVP measurements at anytime during Adam's transplant surgery and if so:

(i) the actual measurements of which you were aware
(ii) when and how you came to know that

(iii) your attitude to such measurements

I was not aware of the actual CVP measurements during the early part of Adam's transplant surgery when I was in contact with the theatre team.

(b) State whether you were aware that Dr. Taylor had not regarded the initial reading of 17 mmHg as accurate and was only relying on the CVP readings for the purpose of their relative change. If so state and explain:

(i) when and how you came to know that
(ii) your attitude to such a response

I was not aware that Dr Taylor did not accept that the initial reading of 17mmHg was accurate until after Adam had left theatre. While I understood Dr Taylor's use of the CVP reading for the purposes of relative change, I was by that time, convinced that Adam had become severely fluid overloaded.

(c) Explain your view of an initial CVP reading of 17 mmHg in the context of Adam's fluid management and what action you consider could and should have been taken in response to it.

Finding a CVP level as high as 17 would initially have indicated that the placement of the CVP line should be checked. I would have been interested to note if a rise in CVP was accompanied by other cardiovascular changes, such as an increase in blood pressure, and I might have considered erecting a CVP line through another venous access if possible. In the context of Adam's fluid management, I would have considered only giving maintenance fluids and losses and indeed perhaps restricting the fluid input as long as blood pressure and pulse were maintained and the evidence of good intra-abdominal circulation was satisfactory.

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

My belief is that in 1995, if an urgent specimen was required to be transported from an operating theatre to the laboratory, that a porter would be made available.

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

I do not believe there was a pneumatic tube system available at that time.

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

(i) identify the type of blood gas analyser which was available at that time
(ii) state where it was located
(iii) state what arrangements would have been required for its use in Adam's transplant surgery

(iv) state the accuracy of the results for sodium compared to
- the static blood gas analyser
- laboratory blood tests

I do not know if a portable blood gas analyser such as an iSTAT machine was available. I cannot identify the type of blood gas analyser which was available at that time, although I am aware there was such an instrument in the intensive care unit adjacent to the theatre. I am unable to answer other questions in relation to the gas analyser.

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

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

The normal turnaround time for laboratory analysis of a serum sodium in 1995, which was non-urgent and during working hours, I believe would probably have been 3-4 hours. This would have been similar out-of-hours, but in the case of urgent specimens, particularly from an operating theatre or intensive care unit where the urgency was made clear, I believe the turnaround time would have been less than one hour. These estimates would need to be verified by the laboratory and portering services.

(43) Answer to Question 14(b) at p.23:

"I cannot say when exactly I arrived in theatre and when I left. I was not in theatre again after 9.00am. Any consultation in relation to Adam's fluid management during the course of his surgery was, most likely, between the anaesthetic staff. My involvement was prior to the surgery to alert the anaesthetic team of the need for electrolyte estimation and the calculated deficit in his normal fluid provision overnight. I cannot say who was in theatre other than my senior colleagues, ie. Mr Patrick Keane, the Transplant Surgeon, Mr Stephen Brown, the Paediatric Surgeon, Dr Bob Taylor, the Paediatric Consultant Anaesthetist, although I was aware there was another senior Registrar Anaesthetist present as well as the nursing staff, whose names I do not know."

(a) Identify to whom you refer as :

(i) *"the anaesthetic staff".*
(ii) *"the anaesthetic team".*

In relation to the anaesthetic staff and team, I communicated directly with Dr Bob Taylor.

(b) State the number of nursing staff in theatre on each occasion that you were present in theatre.

I do not know the number of nursing staff in the theatre when I was present.

(c) State whether there was any consultation in theatre in relation to Adam's fluid management prior to your departure from theatre.

I believe my consultation in theatre in relation to Adam's fluid management only related to the overnight fluid deficit and his normal daily fluid regimen. I was not involved directly in decisions regarding his intra-operative fluid management.

(d) Identify the other "*senior Registrar Anaesthetist*" present in theatre while you were in theatre. In particular, state whether that Senior Registrar Anaesthetist was Dr. Terence Montague or another person.

I do not personally remember the name of the Senior Registrar Anaesthetist, but now believe him to have been Dr Terence Montague.

(e) State whether there was an anaesthetic nurse present in theatre while you were in theatre, and if so, state at what time that nurse was present.

I do not know if there was an anaesthetic nurse present in theatre.

(44) Answer to Question 14(f) at p. 23:

"I was aware that she had summarised his past history a few weeks before for her own information. I informed her of the fluid situation overnight and the fact that things seemed to be progressing slowly but satisfactorily in theatre."

(a) Produce a copy of the summary of Adam's history referred to above.

Dr O'Connor's summary is in the clinical notes (Ref: 058-035-143).

(b) Explain what you mean by "*things seemed to be progressing slowly*" and the basis for that statement.

I do not think there was any particular significance to this phrase, other than to indicate that it was my impression that the operation would continue for some time.

(45) Answer to Question 15(a) at p.24:

"The function of the Renal Transplant Protocol at RBHSC is to provide guidance for all medical and nursing staff involved with the care of children undergoing renal transplantation. The checklist on admission provides an aid memoire for the information and investigations required prior to the transplant. There is a section giving appropriate doses of immunosuppressive drugs and detailed information relating to post-operative management, including the management of fluids, drug treatment and rejection. A copy of the transplant guidelines are placed with the notes of every child undergoing a transplant so that they are available to anyone involved in their care."

(a) State whether the renal transplant protocol at RBHSC was complied with in Adam's case, and if not, specify in what respect the protocol was not complied with.

I believe the transplant protocol was complied with in Adam's case. The protocol recommends fluid expansion may be required prior to release of the arterial clamp. The need for such fluid administration to be determined by reference to the BP and CVP. In retrospect the accuracy of the CVP reading has been questioned. The immunosuppressive drugs employed were methyl prednisolone and Cyclosporin as a decision had been made by the

Nephrologists to move to this regimen.

(b) Identify the particular medical and nursing staff in Adam's case who you consider should have known about and acted in accordance with the Renal Transplant Protocol.

The medical and nursing staff involved in Adam's care following his admission, should have known and acted in accordance with the renal protocol. I believe the junior doctors are Drs Cartmill and O'Neill. I do not know the names of the staff nurses looking after Adam on that occasion, but believe their names have already been communicated to the Inquiry.

(46) Answer to Question 15(b) at p.24:

"In revising the protocol, we consulted protocols from other centres in the U.K. We wanted to ensure that our guidelines were up-to-date or improved to be consistent with best current practice. We wanted to ensure that electrolytes were regularly monitored and that there was some move towards the use of fluids with a higher sodium content perioperatively. The aim of the revision was to improve patient safety."

(a) Identify each "*centre[s] in the U.K*" whose protocol you consulted.

We obtained protocols from The Royal Manchester Children's Hospital, Southmead Hospital Bristol(adults and Children's protocols), The Royal Free Hospital in London, Guy's Hospital London, and Birmingham Children's Hospital. We consulted the Adult Transplant protocol from the Belfast City hospital and a published protocol from UCLA in USA.

(b) State whether you had any discussion within RBHSC, outside the context of renal transplant and/or renal surgery, about the benefits of regularly monitoring electrolytes and the use of fluids with a higher sodium content.

I believe our discussions were mainly within the context of renal and transplant surgery. Initially, we believed that Adam's hyponatraemia was dilutional, related to the volume of fluid administered. Adam's death however, was a major stimulus, particularly after the inquest, for a discussion of the use of N/5 saline in dextrose in general.

(c) If so, identify those involved and when such discussions took place.

The key individuals involved in such discussions would have been myself, Dr O'Connor and Dr Taylor. Dr O'Connor and myself produced new renal transplant guidelines in early 1996, recommending only the use of normal saline intra-operatively during renal transplantation. Dr Gaston chaired a review of electrolyte management in relation to paediatric surgery and anaesthesia in 1996. The finding at Adam Strain's inquest and the identification of the potential risk of hypotonic fluids became a significant issue for discussion within the Northern Ireland paediatric community, resulting in the setting up of the Northern Ireland Regional Paediatric Fluid Therapy Working Group in 2001 by Dr Darragh, the Assistant Chief Medical Officer, on which the Children's Hospital were represented by Dr P Crean and Dr Taylor. I was not included in this Working Group (Ref: 007-042-087). The work of this group resulted in the removal of N/5 saline in dextrose from general use. In March 2007, the National Patient Safety Agency issued an alert (Number 22) on advice on how to reduce the risk associated with the administration of infusions in children, and their recommendations were incorporated into the policy for the administration of IV fluids to children issued by The Belfast Health & Social Care Trust in

2009 and recently updated in April 2011.

The tragic death of Adam Strain therefore ultimately contributed to a change in national policy in relation to the type of intravenous fluids administered to children.

(47) Answer to Question 15(f) at p.25:

"The revised guideline is in relation to alerting consultants to sodium levels less than 133 is to ensure that this is not overlooked, but is analysed and investigated and the transplant team alerted. The consultant would be concerned to identify whether there were any symptoms associated with this level of sodium, whether it was a major variation in the serum sodium level and whether or not there had been any rapid change. Repeat U&E recommendation at the time of theatre is to ensure that the pre-operative fast and IV fluids have not significantly altered fluid or electrolyte balance."

(a) Explain why the 1996 guidelines fixes the threshold for discussion with a consultant at *"sodium levels less than 133"*.

I believe we set this level as a safety mechanism. While it would be standard practice for the consultant nephrologist to check electrolyte and urea investigation results prior to theatre, this threshold was set to ensure that the consultant was informed immediately so that a decision could be made as to whether an intervention was required to adjust the sodium level before proceeding. The DHSSPS Parenteral Fluid Guideline has chosen a lower level of 130 as the trigger for seeking senior advice.

(b) State whether this threshold level was set as a direct consequence of Adam's case.

The threshold level was set as a direct consequence of Adam's case.

(48) Answer to Question 16 at p.26:

"The amendment on the penultimate line of the first page is not in my handwriting. I do not remember why this change was made. I believe it says 'N/5 saline dextrose'. This is the intravenous solution which Adam was receiving on that evening."

(a) Identify the person who made the handwritten *"amendment on the penultimate line of the first page"* of your deposition to the Coroner (Ref: 011-015-109) and state whether you authorised that amendment to your deposition.

I cannot identify the person who made the handwritten amendment but assume it was the Coroner. I have signed the amended deposition but suspect on the day I was more concerned in reading the other extensive additions made to the original statement.

(b) State when that amendment was made, and particularly whether it was made before or after you signed your deposition.

I believe the amendment was made on the day of the Coroner's Inquest, probably before I signed the deposition.

(c) Identify the author of the handwritten notes on your deposition at pages Ref: 011-015-110 to 011-015-112.

Again, I presume that these handwritten notes are those of the Coroner.

(d) State whether you now say that the deposition as amended is correct or incorrect.

I believe that the deposition as amended is correct.

I accept that the handwritten notes (Ref: 011-015-110 to 011-015-112) are a correct record. However, I cannot be sure that the alteration on the first page from Dioralyte to N/5 saline in dextrose (Ref: 011-015-109) is correct. On reviewing the clinical notes, I said that the clear fluids to be given overnight should be Dioralyte (Ref: 058-035-133).

(49) Answer to Question 18(d) at p. 27:

"With reference to the document 060-018-036, I presume this refers to the handwritten addition to the statement in my deposition to the Coroner mentioned under 18b) above and I can only say that this was anecdotal evidence."

(a) You have not adequately answered the question. *"[D]ocument 060-018-036"* is not the handwritten addition to the statement in [your] deposition to the Coroner mentioned under 18b) above. Please answer the question properly including all bullet points.

With reference to the bullet points in question 18(d), page 27 of my previous statement, I did not directly supply this information to Dr Gaston. In my previous answer I was attempting to point out that this information was probably raised from my deposition at the Coroner's Inquest contained in the handwritten addition to my statement there.

(b) State the date when and circumstances in which you first saw *"document 060-018-036"* dated 19 June 1996.

I first saw document 060-018-036 when it appeared on the Inquiry website.

(c) State any input you had into *"document 060-018-036"* and when you provided that input.

Dr Murnaghan and Dr Gaston carried out an internal review of the circumstances around Adam's death as a mortality review on behalf of the Belfast Trust. While I was involved in this process, I believe it concentrated on intra-operative events and to the best of my knowledge, I do not believe I had any direct input into document 060-018-036.

(d) State the source of the information in paragraph 2 of *"document 060-018-036"*.

The information in Paragraph 2 are levels of sodium which Dr Gaston has chosen in defining hyponatraemia. I do not know his source.

(e) State the date when and circumstances in which you first saw document Ref: 060-019-038

I believe I first saw this document when it was placed on the Inquiry website, although I am in agreement with its recommendations and I believe I was aware of them in 1996.

(f) State whether you had any input into document Ref: 060-019-038, and if so, state the date and nature of the input, specifically including the nature of the information you

provided. If you did not have any input, state whether you knew about this document and when and how you first knew of it.

I do not believe I had any direct input into document 060-019-038 and believe I first saw this document on the Inquiry website.

(g) Identify the source of information that led to the change in document 060-018-036 which refers to *"...a number of renal transplants complicated by hyponatraemia leading to death in 10 (reported May 1996)..."* to the statement in document 060-019-038 which refers to *"... perhaps there may have been nine other cases in the United Kingdom involving Hyponatraemia which led to death in renal transplants..."*

In relation to my statement at the Inquest that I believe there had been 9 other deaths from apparently similar causes to that of Adam Strain, I believe the source of this information was a presentation made at a meeting of the British Paediatric Association by D Kate Verrier-Jones. I have previously provided the Inquiry with a copy of a letter which I wrote in 1996 to Dr RJ Postlethwaite, the paediatric representative on the UK Transplant Audit Group, which identifies this source. (ref.HYP B04/1) Following my letter, an audit of all deaths of children following renal transplantation was performed and published (Postlethwaite RJ et al, Paediatric Transplantation 2002:6:367-377).

(h) State the date when and circumstances in which you first saw document Ref: 011-014-107a

I do not know the date or circumstances in which I first saw document Ref: 011-014-107a.

(i) State whether you had any input into document Ref: 011-014-107a, and if so, state the date and nature of the input, specifically including the nature of the information you provided. If you did not have any input, state whether you knew about this document and when and how you first knew of it.

I do not have any recollection of having a direct input to precise content of document Ref: 011-014-107a.

(j) Explain the circumstances by which document Ref: 011-014-107a with its reference to *"perhaps there may have been nine other cases in the United Kingdom involving hyponatraemia which led to death in patients undergoing renal transplantation..."* came to be provided to the Coroner during Adam's inquest.

I do not know the circumstances by which document 011-014-107a came to be provided to the Coroner during Adam's inquest.

(50) Answer to Question 21(b) at p.29:

"[T]he stimulus for commencing renal transplants at RBHSC"

(a) State when renal transplants commenced at the RBHSC

The first paediatric transplant was carried out at RBHSC in June 1990.

(b) State whether there has been any audit or assessment of renal transplant surgery at the RBHSC or of Belfast as a renal transplant centre. If so,

(i) state when such audits or assessments occurred (in both cases)
(ii) who conducted them
(iii) your role, if any, in them
(iv) identify any report resulting from such audits and assessments, and if available, provide a copy

All renal transplants carried out in Belfast are monitored as part of a national audit of graft survival, patient survival, and the influence of such factors such as immuno-supression regimens. In relation to the period when Adam Strain received his transplant, an audit of all paediatric renal transplants in Northern Ireland between 1984 and 1998 was carried out and published in May 2000 by Dr Clifford Mayes, Senior Registrar, and Dr Maurice Savage, Consultant Nephrologist. This audit demonstrated that results in the Belfast centre during that period were comparable with any other centre in the United Kingdom. A copy of this audit is attached (See Appendix [4]). The results of the National Audit of Centres, including graft and donor survival rates, are published by the UK Transplant Service (See Appendix [5]).

(51) Answer to Question 24(a) at p.30:

"As the single Consultant with overall responsibility for Adam Strain's medical treatment and management during the five years of his life, all the medical record entries made in his notes during hospital admissions and at out-patient visits were made either by me or under my direction by one of my junior colleagues. The exceptions to this will be entries made by members of the surgical team, bearing in mind that he had 20 operations, and which are listed in a separate document provided by the Belfast Trust. There are therefore many hundred entries spread across 10 sets of clinical notes."

(a) Identify precisely on Adam's medical notes and records the entries in your handwriting.

Please see attached Appendix [6].

(b) State the location/s of those *"10 sets of clinical notes"* on 26th and 27th November 1995.

I cannot be certain at this time as to where exactly all the 10 sets of clinical notes were, but expect they would have been initially in the medical records department of the Children's Hospital.

(c) Describe how those *"10 sets of clinical notes"* could have been retrieved on 26th and 27th November 1995 for the purposes of pre-transplant preparation.

These 10 sets of clinical notes could have been requested and brought to the ward from the medical records department.

(d) State how long you think it would have taken to retrieve those *"10 sets of clinical notes"* if an out of hours request was made.

Retrieving medical notes from the medical records department for a child undergoing surgery, could I would expect have been achieved within one hour from the medical records department.

(e) Identify the clinic notes that were provided to Dr. Taylor for the purpose of pre-

transplant preparation.

I cannot remember at this stage if all Adam's 10 sets of clinical notes were provided to Dr Taylor.

(52) Answer to Question 25 at p. 30:

"Adam had episodes of hyponatraemia prior to the events of 25-27 November 1995. These developed and were resolved relatively slowly, usually by receiving oral tube feeds with added sodium supplements. On such occasions he was asymptomatic and came to no harm."

(a) State whether you conveyed this information to Dr. Taylor prior to Adam's renal transplant surgery, and if so, state when and in what circumstances. If you did not do so, please explain why not.

I believe I did communicate to Dr Taylor the fact that Adam had a tendency to develop low sodium levels, which were addressed by the nature of his tube feeds and the addition of sodium bicarbonate and saline to those feeds.

(53) Answer to Question 25 at p. 30:

"Neurological complications of hyponatraemia generally occur when this develops acutely during intravenous fluid treatment and when the serum sodium falls quickly and to an extremely low level (Friedman and Ray, Paediatric Nephrology (2008) 23: 677-680)."

(a) Explain what you mean by *"this develops acutely"*

The phrase "develops acutely" refers to a fall in plasma sodium from normal to less than 130mmol per litre in a short space of time. Some would regard this as a fall greater than 5mmol in 24 hours, therefore, a fall to 130 or less in 48 hours would be acute hyponatraemia, and if such a fall occurred in 24 hours or less, this would be regarded as a rapid fall.

(b) Explain what you mean by *"when the serum sodium falls quickly"* and specify the rate of fall to which you refer.

The current DHSSPS guideline instructs junior doctors to seek senior advice if there is a fall in sodium >5 in 24 hours.

(c) Explain what you mean by *"to an extremely low level"* and specify the level to which you refer.

"An extremely low level" would be a sodium of 125mmol per litre.

(54) Answer to Question 25 at p. 30:

"The standard and accepted maintenance of intravenous fluid for children in 1990-1995 and for a long time subsequently, was N/5 (0.18%) saline in dextrose (Kannan et al, Pediatric Nephrology (2010) 25: 2303-2309).

(a) Explain what you mean by *"and for a long time subsequently"* and specify the length of time to which you refer.

"For a long time subsequently" certainly means to the early years of the 21st Century. A Viewpoint article in The Lancet 2003; 362:1320-23, states that intravenous fluids are used for many sick and injured children. Such fluids generally used are 0.18% or 0.2% saline with 5% dextrose. The Standard Paediatric Textbook of Paediatrics in the UK by Forfar & Arneil in their 6th Edition 2003, indicates 0.18% saline with 4% dextrose and 10mmol of KCL (potassium chloride) on page 585 for maintenance fluid and electrolyte requirements.

(55) Answer to Question 25 at p.30:

"The paper published by Arieff (British Medical Journal (1992), 304, 1218-1222)..."

(a) State what you considered to be the significance of Arieff's paper to fluid management of children generally, and explain the basis of your view.

The paper published by Arieff in 1992 in the British Medical Journal is highly significant in that it alerted paediatricians to the dangers of intravenous fluids, even in relatively well children undergoing surgery, due to the release of anti-diuretic hormone. This paper sparked the debate in relation to the ideal intravenous fluid to be administered to children in hospital and has resulted ultimately in a withdrawal of N/5 saline in dextrose as an intravenous fluid for children.

(56) Answer to Question 25 at p.31:

"Even with the developments since Adam's case, these patients remain extremely difficult to manage and fatalities still occur even in the best Centres..."

(a) State whether you considered prior to 27th November 1995 whether Adam's renal transplant should take place in another Centre, and if so which Centre, and what happened as a result of your view. If you did not consider this, state the reasons why not.

I did not consider referring Adam to another centre for a renal transplant prior to November 1995. I believed that the success rate with renal transplants in Belfast was similar to that in any other centre. In more recent years we have considered such referrals, and in special circumstances, have referred children to The Hospital for Sick Children at Great Ormond Street.

(57) Answer to Question 25 at p.31:

"The intense debate resulted in the discontinuation of the use of hypotonic solutions such as N/5 (0.18%) saline in dextrose in Northern Ireland..."

(a) State whether the use of *"N/5 (0.18%) saline in dextrose"* has been discontinued at RBHSC, and if so, from when and in which departments. If not, state the reasons why not.

The use of N/5 saline in dextrose has been discontinued from general use at RBHSC since 2007. This fluid can be used in special circumstances on the order of a consultant in the paediatric intensive care unit or by a consultant nephrologist in the management of certain renal conditions (Standards & Guidelines Committee Policy of IV fluids for children from 1 month to 16th birthday, Revised April 2009).

(58) Answer to Question 25 at p.31:

"The renal team at the Royal Belfast Hospital for Sick Children uses only normal saline for intravenous replacement of fluid deficit and N/2 saline in 2.5% dextrose for maintenance therapy."

(a) State when the renal team at the RBHSC:

(i) first commenced using only *"normal saline for intravenous replacement of fluid deficit and N/2 saline in 2.5% dextrose for maintenance therapy"* and the reasons for this change.

The renal team at RBHSC changed to using normal saline for routine intravenous fluid deficit and to half normal saline in dextrose for maintenance therapy in 2005.

(ii) ceased using N/5 (0.18%) saline in 4% dextrose and the reasons for this change.

We ceased using N/5 saline in dextrose because of increasing evidence that the use of such fluid carried a significant risk of hyponatraemia.

II. ADDITIONAL QUERIES

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

I was not aware of any application by the RBHSC to be an accredited institution with the King's Fund Organisational Audit in 1995.

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

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

I was aware that there was a review of Adam's death within the anaesthetic directorate which resulted in the recommendations in documents 060-018-036, 060-019-037,060-019-038 and in document 011-014-107a. While these recommendations concur with conclusions and suggestions made by myself and Dr O'Connor, I do not believe we were directly involved in the discussions. I therefore cannot state who did participate in them.

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

I was not involved in discussions but concurred with the recommendations in 60 (a).

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

I do not know why I was not involved in these discussions.

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

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

I do not have any recollection of audit procedures in 1995. I have attached the current procedure for clinical audit in the Belfast Trust in Appendix [6].

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

I have no documents in relation to a clinical audit of Adam's case. In 1995, to my knowledge, clinical audit and mortality conference proceedings were not minuted. As a result of the review of Adam's case, new renal transplant guidelines were drawn up in 1996 to exclude the use of N/5 saline in dextrose intra-operatively. It has become our practice to draw up a clinical summary of relevant details to be available to the transplant surgeon on each patient on call for transplant, and also for the transplant surgeon to meet the patient and family in advance of the proposed transplant. Dr Gaston's group has made recommendations in relation to the monitoring of electrolytes before and during this type of surgery.

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

I believe if a similar tragedy to Adam's occurred in 2011, a more formal audit would be instigated by the Trust. I would certainly consider publishing the details of the case in a medical journal if there were lessons that might be learnt in the wider paediatric community.

(62) Describe the procedure for discussions of deaths amongst medical personnel (e.g. 'death meetings' / 'morbidity and mortality meetings') at RBHSC in November 1995 and identify any relevant documents

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

I am not aware of any document which describes current procedure for discussion of deaths in RBHSC. However, it has been the practice that all deaths are discussed at the monthly morbidity and mortality meeting held in the hospital.

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

I am not certain that Adam's case was discussed at the mortality meeting as no records are kept. Certainly, events surrounding Adam's death were the subject of detailed discussion in which I participated.

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

I was not involved at any stage, to the best of my knowledge, with the clinical negligence claim that was pursued following Adam's death.

(64) State whether you communicated personally with Adam's family following the inquest into his death. If so, state what you discussed and when you did so.

I did communicate personally with Adam's family on several occasions following the inquest into his death. I met with Debra Strain on several occasions and visited with her and her parents at their home. We certainly discussed the cause of Adam's death from dilutional hyponatraemia on several occasions over a number of months. My contact with Ms Strain at that time was in a supportive role because of her enormous loss and bereavement. My memory is that her parents were extremely concerned about her at that time and particularly because she would seek no help, either from her family doctor or from bereavement counselling. They believed that being able to talk to me about Adam because I had looked after him for so long was beneficial, and so on occasions they invited me to call at their home.

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

(a) present using the "+" symbol and

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

See attached Appendix [8].

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

Signed: Maurice Savage **Dated:** 28/9/11

APPENDICES LIST

List of attached documents:

1. Renal Services Review 2002, DHSSPSNI (1(f) refers)
2. RBHSC Renal Transplant Guidelines, 1996 (2(j) and 13(a) refer)
3. Standards and Guidelines Committee document (2(k) refers)
4. Paediatric Renal Transplantation in Northern Ireland (1984-1998), Ulster Medical Journal (50(b) refers)
5. Renal Transplant Audit (UKTSSA) 1984-1993 (ISSN1358-653x, page 83-87) (50(b) refers)
6. Answer to Question 51(a): entries in Adam's medical notes
7. Paediatric Audit Strategy document (61(a) refers)
8. Answer to Question 65: Table for Paediatric Renal Transplant

Department of Health, Social Services and Public Safety
An Roinn Sláinte, Seirbhísí Sóisialta agus Sábháilteachta Poiblí

Renal Services Review 2002

INVESTOR IN PEOPLE

8. PAEDIATRIC RENAL SERVICES

8.1 Introduction

8.1.1 Paediatric nephrologists and their teams look after children with a variety of both acute and chronic, renal conditions. Treating children with renal disorders and providing the necessary support for their family, demands extensive input from a variety of professionals, including doctors, nurses, psychologists, social workers and dieticians.

8.1.2 Pressures on the service come from increasing public and professional expectation, and technical advances enabling infants and young children to begin renal replacement therapy where previously this would not have been possible. Teams are also increasingly involved in counselling parents on the management options and prognosis for children diagnosed with renal abnormalities in the pre-natal period.

8.2 Epidemiology and Future Trends

8.2.1. At November 2002, there are five children receiving haemodialysis, five receiving peritoneal dialysis, and 20 transplanted patients under 16 years of age. It is anticipated that seven children in chronic renal failure will require dialysis within the next six months.

8.2.2 It is difficult to forecast trends in the incidence and prevalence of end stage renal disease in children in Northern Ireland, due to the small numbers of children involved, and the potential for year to year variation due to chance.

8.2.3 Data from the UK and Ireland suggests a change in the proportion of children on the various treatments for end stage renal disease end stage renal disease.[22] The proportion of children with successful kidney transplants has risen from 66% in 1992 to 75% in 2000. For those on dialysis the proportion having haemodialysis has increased from 26% to 41%. Under the age of five years there are more dialysis

patients than transplant patients, beyond this age there is a ratio of 4:1 transplanted to dialysis patients.

8.3 Local Services

8.3.1 Paediatric nephrology services are provided on a regional basis at the Royal Belfast Hospital for Sick Children. At present the service is unable to provide outreach clinics. Consultant renal physicians with the support of a multidisciplinary team deliver the service.

8.3.2 Medical care at both inpatient and outpatient levels is provided by consultant paediatric nephrologists. This is in contrast to many other specialties where a larger proportion of care is provided by junior staff. There are currently two (1.6 whole time equivalents WTE) consultant paediatric nephrologists in post. The European Working Hours directive is likely to impact on the viability of the present 1 in 2 out of hours on-call rota.

8.3.3 The present funded trained paediatric renal nursing establishment is 4.67 whole time equivalent. Trained paediatric renal nurses are needed for the following:

- Transplant patients;
- Peritoneal dialysis new starts, and complications to existing patients;
- Existing haemodialysis patients;
- Acute renal failure;
- Parent and patient education and support;
- Telephone support to home dialysis families.

8.3.4 The renal technical service at the Belfast City Hospital provides support for dialysis equipment at the Royal Belfast Hospital for Sick Children. This includes ordering of supplies such as artificial kidneys and other consumables. Technical service management are happy for this arrangement to continue.

8.3.5 Psychologists advise on the management of problems such as behavioural difficulties, coping with transplantation, procedure-related phobias, emotional liability issues, and dysfunctional family dynamics. Graft rejection due to non-compliance, anger management, and preparation for transfer to adult services are particular problems for adolescents. Currently the paediatric renal service has funding for 0.1 WTE psychologist. An expanded service would allow earlier identification of vulnerable children, adolescents, and families, with the prospect of intervention before coping skills are challenged.

8.3.6 Social workers advise families and patients on their rights and entitlements, and liaise with a variety of statutory and voluntary bodies on their behalf. In addition to providing general psychosocial support to families and patients, they also provide specific support on issues such as counselling on long-term treatment options and prognosis, and on preparation for transplant. They need to be able to visit families at home, and to attend outpatients and wards. The current social work establishment is 0.5 WTE. The main identified gap in the service is a lack of interviewing space close to the ward.

8.3.7 Dieticians advise on the dietary modifications required for children with renal disorders, taking a major role in the management of children, on dialysis who require enteral feeding. They also have a role in training parents, home visits, school liaison, and in ensuring regular monitoring of children's diets. At present the dietetic service is funded for 0.2 WTE. This does not allow time for dietary monitoring, or for participation by the dietician in outpatients. Audit and research are currently not possible.

8.4 Accommodation

8.4.1 The paediatric renal service cares for between two and five patients in the hospital ward at any one time, and is currently being provided from within three side rooms on Musgrave ward, a general medical paediatric ward.

8.4.2 The 1995 Regional Review of Renal Services stated that nursing immune-compromised renal patients in this general medical ward environment, with the attendant risks of cross infection, was unsatisfactory.

8.4.3 The development of an appropriate ward environment for renal services cannot easily be addressed within the current physical layout of the Royal Belfast Hospital for Sick Children. Ideally, the Royal Hospitals Trust would see a solution arising within the planned Phase 2 build. The Trust is preparing an Outline Business Case for the replacement of ward areas. However, the Trust recognises that a new renal unit is several years away.

8.4.4 The only interim step available is the refurbishment of a non-clinical area in Royal Belfast Hospital for Sick Children, providing an eight-bedded area, to facilitate the relocation of the renal service. Preliminary estimates are that this would incur capital costs of £350,000 and annual revenue costs of £465,556. This solution relies heavily on the recruitment of more trained paediatric nurses. Given current difficulties it may be difficult to implement.

8.5 Urodynamics service

8.5.1 Not only are urodynamic investigations essential for the assessment of children's suitability for transplantation, but in some cases they may also identify those children where surgical treatment might prevent the development of end stage renal disease altogether.

8.5.2 This service should be maintained and developed to reflect future needs.

8.6 Radiology service

8.6.1 There is now a waiting list of over one year for some non-urgent kidney scans. Apart from the clinical issues this is curtailing the efficiency of the outpatient system and creating more review appointments. In addition, indirect cystourethrography is not available in Royal Belfast Hospital for Sick Children. This means that other more invasive techniques are used instead. While some of these services are not truly regional inasmuch as they are provided in other Board areas, they should also be available for Eastern Health and Social Services Board patients.

8.7 Recommendations

23. A business case should be prepared by the Royal Group of Hospitals Trust for the refurbishment of a non-clinical area in Royal Belfast Hospital for Sick Children to allow improved separation of immune-compromised renal patients from patients in the general ward. Preliminary estimates indicate that this development could be costly in both capital and revenue. There may be particular difficulties in recruiting sufficient paediatric nurses to run the new bed area. An assessment of the feasibility of the project should therefore be set out in the business case.

24. An additional paediatric nephrologist should be appointed. This should allow delivery of outreach clinics. In light of the on-call commitments of this service, over time a fourth post should be funded. The daytime job plan of this post may combine general paediatric and nephrology duties.

25. The existing specialist registrar post should be sufficient to ensure applicants for both new posts and possible retirements. However,

steps should be taken to ensure that daytime duties are focussed primarily on nephrology patients rather than general paediatrics. This may require the general paediatric workload to be taken over by expected growth in the specialist registrar complement in Royal Belfast Hospital for Sick Children.

26. The nursing complement should be increased to 7 WTE to provide a trained paediatric renal nurse available at Royal Belfast Hospital for Sick Children, 24 hours per day. In addition, one nurse per year for the next three years should be trained, to increase the pool of trained paediatric renal nurses on site. The situation should be reviewed in three years time.

27. The psychology service should be expanded to 0.5 WTE. While this post is primarily for the care of renal patients, this level of manpower should also allow some input to children with diabetes, with a view to the longer term prevention of renal disease.

28. An additional 0.5 WTE dietician should be appointed. In addition, the Trust should consider measures at an operational level to ensure that renal dietetic, psychology and social work expertise is sufficiently available within Royal Belfast Hospital for Sick Children to provide cross cover in the event of staff absence or leave.

29. The urodynamics service should be maintained and developed, subject to business case appraisal.

9. STAFFING IMPLICATIONS FOR ADULT SERVICES

9.1 Introduction

9.1.1 This section outlines the current position for key staff involved in delivering adult renal services. It provides benchmarking against workforce ratios in the UK and against national body recommendations. The staffing requirements for paediatric services are set out in section 8. All other staffing recommendations are set out in Table 6.

9.1.2 For many of the professional groups within renal services the current numbers in post are similar to national recommendations. Consequently it is recommended that expansion in staff numbers, for these groups, should correspond with expansions in services as laid out in the review report.

9.1.3 However, there are a number of key staffing issues, upon which future expansion is critically dependent.

9.2 Nursing Staff

9.2.1 To provide an optimum level of care for the expansion of the renal dialysis service, it is estimated that 175 WTE (whole time equivalent) additional nursing staff will be required between 2002 and 2010. At the current skill-mix, this equates to 123 WTE qualified nurses and 52 WTE dialysis assistants. The nursing figure includes provision for a qualified nurse in each of the existing local renal renal units to provide education, training and support for patients on peritoneal dialysis.

9.2.2 In addition, to provide nurse-led clinics and assistance at consultant led clinics for vascular access, anaemia management, pre-dialysis etc. 1.3 WTE nurses will be required at the regional unit and 0.5 WTE at each of three existing local renal units – a total of 2.8 WTE.

RBHSC RENAL TRANSPLANT GUIDELINES

CHECK LIST ON ADMISSION

A) HISTORY:-

Function of native kidneys - volume output.
Recent contact with infectious diseases.
When last dialysed.
Vaccination history.
CMV status donor/recipient.
Cytotoxic antibody status.
Tube feeds - what and how much.
What central line sites used previously.
List drugs.

B) EXAMINATION:-

State of nutrition.
State of hydration.
BP
Height and weight, surface area.
Catheter exit site appearance.

C) INVESTIGATIONS (insert peripheral cannula at same time)

Clotted sample - 5 ml by taxi to Ward 11N, BCH for tissue typing X-match (telephone 7-111-2455).
FBP, DWCC, coag screen, U/E, creat, Ca, albumin.
Group and X-match 4 units WBC depleted CMV -ve blood.
Virology for Hep A, B and C, CMV, measles, chickenpox, HIV, EBV.
PD fluid and urine for culture.
Urine for U/E and creatinine.
CXR
ECG if on antihypertensives.

PLAN:-

1. Fast and consent.
2. Shower.
3. Dialysis if k+ > 5.
4. Peritoneal Vancomycin loading dose (500 mg/l) Leave x 4 hours and drain pre Theatre.
5. If prolonged fast - maintenance IV fluids (give insensible losses (= 300 ml/m^2) and output) as 0.18% saline, 4% dextrose. D/W Consultant if Na < 133. Repeat U/E at time of going to Theatre.

CMV +ve donor CMV-neg rec → ~~gang~~ IV gang x 14d
and valganciclovir

(donor/recip CMV → oral acyclovir).

6. Acyclovir - if either donor or recipient CMV positive.
   800 mg PO 2-6 hours pre-op.
   800 mg PO 24 hours post-op.

   Thereafter according to GFR

> 25 ml/min/1.73	6 hourly	800 mg PO
10-25 ml/min/1.73	8 hourly	800 mg PO
< 10 ml/min/1.73	daily	800 mg PO
Dialysis dependent	12 hourly	800 mg PO

   (Half dose in < 2 years old)

7. Complete "Check List" for Theatre.

IMMUNOSUPPRESSION

TAC

1. CYCLOSPORIN
   Start ~~3~~ mg/kg/12 hrs/IV by syringe pump infusion pre-op.
   (Alternative if decided by Consultant =
   ~~3~~ mg/kg IV ~~slow~~ bolus over 4 hours pre-op or
   10 mg/kg orally 4 hours pre-op)

2. AZATHIOPRINE
   2 mg/kg/IV in 50 ml saline and given over 20 min pre-op.

3. For highly sensitized patients, ie > 70% cytotoxic antibiotics
   - Antithymocyte globulin (see separate protocol).

IN THEATRE

Assess hydration, check electrolytes and ABG x 2 hourly.
IV Augmentin on induction.
S/C Heparin with surgeons consent after induction.

< 15 kg	1000u tds
15-20 kg	1500u tds
20-40 kg	2500u tds
> 40 kg	5000u tds

Triple lumen CVP catheter.
IA line in small children.
If Hb < 10 g/dl give packed cells to bring it up to 10 g/dl.
Start Dopamine 2-3 ~~mg~~ µg/kg/min.
Use N.saline, plasma, or blood (as appropriate) to raise CVP to 8-10 cm mmHg prior to removal of vascular clamps. Keep CVP here.

10-15 MINS PRIOR TO
RELEASE OF CLAMPS - 0.5 g/kg (2.5 ml/kg) 20% Mannitol 35 mls
(alternative 4 mg/kg Frusemide)

- 10 mg/kg Methylprednisilone (max 500 mg)

POST-OPERATIVE

1. FLUIDS

Replace urine output and insensible losses (300 ml/m^2 /day) EACH HOUR as 0.45% saline 2.5% dextrose (subtract volume of infusions).

Boluses of N.saline or HPPF (5-10 ml/kg) over 20 mins to maintain CVP and BP.

2. OBSERVATIONS

a. CVP between 5-10 mmHg.
b. BP decided on individual basis.
c. Optimal urine output to be decided on an individual basis. In polyuric patients this will be around 4 ml/kg/hr initially, falling to 2 ml/kg/hr when stable. In previously anuric patients far lower outputs may be acceptable if ATN has occurred. Check transplant troubleshooter for management guidelines on output and BP.

3. DRUGS

Immunosuppression

a. Cyclosporin 6 mg/kg/24 hrs written up as continuous infusion via syringe pump 3 mg/kg/12 hrly (not stable for longer). This will be converted to Cyclosporin 12 mg/kg/day orally given as bd dosage. Stop infusion 12 hours after first oral dose.

b. Methylprednisilone 60 mg/m^2/day as bd dose for first 5 days and then reduce (see separate sheet).

c. Azathioprine 1 mg/kg/day from D1 post-op - IV or oral, for monitor WCC. Stop after one month if no rejection.

Prophylaxis

d. Dopamine 2-3 mcg/kg/hr.

e. Ranitidine 1 mg/kg bd IV, oral 2 mg/kg bd (Until minimum steroid dose achieved)

f. Nifedipine 5-20 mg bd as Cyclosporin toxicity prevention.

g. Septrin 120-480 mg orally bd Mon, Wed, Fri for 3-6 months.

h. Heparin 1000-2500 s/c tds for 5-10 days.

i. Acyclovir if CMV +ve donor or recipient (see above).

Analgesia

j. Epidural
or
k. Morphine 10-20 mcg/kg/hr infusion (half BW (kg) in mg in 50 ml at 1-2 ml/hr).

INVESTIGATIONS

1. U/E, creatinine, glucose, Ca x 6 hourly for 24 hours.
   x 12 hourly next 24 hours.
   x daily thereafter (+ phosphate).

2. Doppler renal USS post-op if possible and repeat PRN (? daily)

3. FBP, DWCC, (and CD3 count if on ATG) daily.

4. CXR daily for 2-3 days.

5. Urine - culture, U/E and creatinine daily.
   - protein/creatinine ratio x twice daily.

6. Cyclosporin levels analysed Tue and Fri (RVH Ext 3334). When on oral drugs send daily for 10 days and thereafter Tue and Fri.

IMMUNOSUPPRESSION POST TRANSPLANT

1. STEROIDS

Day 1-5	Methylprednisolone 60 mg/m^2/day as bd dosage x 5 days (may be changed to same dose oral Prednisolone as soon as tolerated).
Day 6	Prednisilone 30 mg/m^2/day as 2 divided doses.
Day 14	Prednisilone 20 mg/m^2/day as 2 divided doses.
Day 21	Prednisilone 10 mg/m^2/day as 2 divided doses.
Week 4-8	Prednisilone 10 mg/m^2 DAILY as one daily dose.
Week 8-12	Prednisilone 5 mg/m^2DAILY.
Week 12+	Prednisilone 10 mg/m^2 alternate days.

2. AZATHIOPRINE

If no severe rejection STOP at 4-6 weeks. Do not give if neutrophils < 1000 or total WCC < 3000.

3. CYCLOSPORIN

Always as NEORAL

Levels -	Weeks 0-4	150-250 ng/ml
	Weeks 4-12	150-200 ng/ml

FOLLOW UP

After discharge	-	alternate days x 1 week
Until week 6	-	twice weekly
Week 6-10	-	weekly
Week 10-12	-	fortnightly
> 3 months	-	monthly
> 1 year	-	6-8 weekly

NB. See within 1 week of any DOSE CHANGES

REJECTION

ASSESSMENT OF REJECTION

> 10% rise in serum creatinine is a significant change. It could be due to:-

1. Laboratory error.
2. Rejection.
3. Cyclosporin toxicity.
4. Other drug toxicity (especially Acyclovir).
5. Infection (especially UTI).
6. Obstruction - exclude with renal USS.

All such rises in creatinine should be reported to the Consultant and repeated immediately. If a 10% rise is confirmed and rejection suspected then initial treatment would be:

Methylprednisolone 15 mg/kg/IV for 3 days (maximum 500 mg).

This should only be prescribed after discussion with Consultant.

Other causes of a rise in creatinine should be excluded and diagnosis confirmed whenever possible with a renal biopsy.

For patients who have received renal transplant > 1 month previously, oral Prednisolone 3 mg/kg/day is given for 3 days (maximum 150 mg).

ANTI-THYMOCYTE GLOBULIN (MERIEUX-RABBIT)

Given for steroid resistant rejection or as prophylaxis when recipient > 75% cytotoxic antibodies or second transplant when first graft lost early with rejection.

Test dose: 0.1 ml (0.5 mg) in 10 ml N.Saline over 1 hour via central line.

TRANSPLANT TROUBLESHOOTER

OUTPUT

If urine output falling < 2 ml/kg/hr give volume to correct low BP or CVP.

Volume — 5-10 ml/kg/stat of N.saline or HPPF
(or blood if appropriate)
May need repeated frequently in first 24 hours leading to positive fluid balance ≥ 1-3 litres.

BP

If high - Hydralazine 0.2 - 1.0 mg/kg/IV stat followed by hourly infusion at same rate.

If low - Volume or Dobutamine (0-20 mg/kg/min)

TEMPERATURE

After first 24 hours may signify rejection.
Check creatinine, blood cultures, urine culture, CXR.

SUDDEN ONSET OLIGURIA/ANURIA

Catheter blocked?

Anastomotic leak?

Urine leak?

IF IN DOUBT CALL CONSULTANT NEPHROLOGIST

NURSING CHECK LIST FOR TRANSPLANT

NAME:

Height

Weight

BP

MSU and urine U/E

Shower

PD sample for microscopy and culture

PD Vancomycin 500 mg/l and run in usual fill volume and drain one hour pre theatre.

Pre-op Cyclosporin

Azathioprine

? ATG

Acyclovir if CMV +ve donor or recipient

ANAPHYLAXIS treated with:

Hydrocortisone 100 mg IV
Chlorpheniramine 5-10 mg IV
Adrenaline (0.01 ml/kg of 1 in 1000, 1 m)

Prior to theraputic dose give Chlorpheniramine IV and Hydrocortisone IV.

Theraputic Dose:

$\leq$ 30 kg - 2.5 mg/kg/day

> 30 kg - 1.25-2.5 mg/kg/day

Diluted in 100 ml saline central line over 8 hours.
Chills, fevers and arthralgia common.

ATG Monitoring

Aim absolute lymphocyte count 200-400 (omit if < 200).

CD3 count daily

(Send 0.5 ml EDTA blood to RVH immunology,
arrange with extension 2689,
ask for lymphocyte markers profile I which includes CD3).

Aim level 100-300 (omit if < 100).

Updated Sept 96
M Savage/M O'Connor

Standards and Guidelines Committee

Policy for the administration of intravenous fluids to children aged from 1 month until the 16th birthday: reducing the risk of hyponatraemia.

Summary	This policy outlines the BHSCT approach for administration of intravenous fluids to children aged from 1 month until the 16th birthday with particular reference to reducing the risk of hyponatraemia. It maps the advice issued in March 2007 from the National Patient Safety Agency (NPSA) and September 2007 from the Northern Ireland Regional Paediatric Fluid Therapy Working Group on how to reduce the risks associated with administering intravenous infusions to children. This is fundamentally a document aimed at prevention of hyponatraemia and not treatment.
Purpose	To improve the safe use of intravenous fluid in children and reduce the risk of hyponatraemia.
Operational date	March 2008
Review date	March 2010
Version Number	V4
Supersedes previous	V3
Director Responsible	Medical Director
Lead Author	Dr. Peter Crean
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Reference Number	
Supercedes	N/A

Date	Version	Author	Comments
25 August 2009	V 3.1	JR Johnston	Draft version 3
14 September 2009	V 3.2	JR Johnston	Minor RMcL amendments
16 September 2009	V 3.3	JR Johnston	8.3.4; Appendix 6 changes Final Draft for RQIA
17 September 2009	V 3.4	JR Johnston	4.1; 8.4 - DKA Fluid chart change
17 September 2009	V 3.5	JR Johnston	Appendix 4 changes
February 2010	V 3.6	JR Johnston	Trigger list

Policy Record

		Date	Version
Author (s)	Approval	27/03/2008	1.2
Director Responsible - Dr A Stevens	Approval	27/03/2008	1.2

Approval Process – Trust Policies

Policy Committee	Approval		
Executive Team	Authorise		
Chief Executive	Sign Off		

Approval Process – Clinical Standards and Guidelines

Standards and Guidelines Committee	Approval		1.2
Policy Committee	Approval		
Executive Team	Authorise		
Appropriate Director	Sign Off		

Summary

Reference No: SG001/08

Title:
Policy for the administration of intravenous fluids to children aged from 1 month until the 16th birthday: reducing the risk of hyponatraemia.

Purpose:
To improve the safe use of intravenous fluid in children and reduce the risk of hyponatraemia.

Objectives:
This Policy sets out recommended practice for everyone who looks after children receiving intravenous fluids. It is based on regional and national guidance, ongoing clinical audit, published literature and is also aimed at specifically reducing the risk of hyponatraemia.

It should be considered alongside the guidance from the National Patient Safety Agency Patient Safety Alert 22[1], and the Regional Paediatric Fluid Therapy Group wallchart[2].

Policy Statement(s):
1. The Paediatric Parenteral Fluid Therapy wallchart[2] forms the basis of BHSCT guidance on fluid prescription in paediatric patients aged from 1 month until the 16th birthday.
2. Sodium chloride 0.18% with glucose 4% will be withdrawn from general use in all BHSCT ward areas that treat children and the availability of these fluids will be restricted to critical care areas and other specialist wards such as renal, liver and cardiac units.
3. This policy and wallchart will be disseminated throughout the BHSCT.
4. Information about the availability of infusion fluids throughput the BHSCT will be attached to the Paediatric Fluid Guideline wall chart[2].
5. A new fluid prescription/ balance chart will be developed for the prescription of fluids for all children treated in the BHSCT.
6. All staff involved in prescribing, administering and monitoring IV fluids to such children will be made aware of this policy and the Paediatric Parenteral Fluid Therapy wallchart[2] through the BHSCT intranet and Service Group dissemination.
7. The BHSCT will implement the following governance measures – incident reporting using a set of reporting 'triggers' and formal auditing.

Chief Executive/ Director *(delete as appropriate)*	**Author**
Date:	**Date:**

Contents Page:

Full Description

Reference No: SG001/08

1. ***Policy for the administration of intravenous fluids to children aged from 1 month until the 16th birthday: reducing the risk of hyponatraemia.***

2. **Introduction:**

The development of fluid-induced hyponatraemia in the previously well child undergoing elective surgery or with mild illness may not be well recognised by clinicians.[1]

Since 2000, there have been four child deaths following neurological injury from hospital-acquired hyponatraemia reported in the UK.[1] International literature cites more than 50 cases of serious injury or child death from the same cause, and associated with the administration of hypotonic infusions.[1]

In March 2007 the National Patient Safety Agency (NPSA), with Alert 22, issued advice on how to reduce the risks associated with administering infusions to children[1].

In April 2007, with DHSSPSNI circulars[3,4], NHS organisations in Northern Ireland were tasked to produce and disseminate local clinical guidelines for the fluid management of paediatric patients based on the suggested NPSA guidelines template. The Northern Ireland Regional Paediatric Fluid Therapy Working Group produced an intravenous fluid clinical guideline in accordance with NPSA guidance[1]. This was disseminated to each HSC Trust for local implementation and monitoring.

In February 2009 the Regulation and Quality Improvement Authority (RQIA) published an independent review "*Reducing the risk of hyponatraemia when administering intravenous infusions to children*" which dealt with the implementation of recommended actions outlined within the NPSA Alert 22 and dissemination of the clinical guidelines / wall chart throughout HSC Trusts and independent hospitals. (see appendix 7.)

This document, using both the NPSA guidance and the RQIA recommendations, outlines the BHSCT policy for administration of intravenous fluids to children aged from 1 month until the 16th birthday with particular reference to reducing the risk of hyponatraemia; it is fundamentally a document aimed at prevention of hyponatraemia and not treatment.

3. **Purpose:**

To improve the safe use of intravenous fluid in children and reduce the risk of hyponatraemia.

4. **The scope:**

4.1 Applicable to all children more than 1 month and until their 16th birthday throughout the Belfast Health and Social Services Trust (BHSCT).

It is relevant for all general inpatient areas that treat patients from this age range (even if it is only occasionally) and includes the post-operative scenario, emergency departments, day case departments and the ambulance service.

This policy (and attendant fluid prescription chart) is not intended to apply to paediatric

and neonatal intensive care units, specialist areas such as renal, liver and cardiac units where it is used to replace ongoing losses of hypotonic fluids, or those suffering from burns or diabetic keto-acidosis (DKA) where hypotonic solutions may have specialist indications.

Children receiving long term Total Parenteral Nutrition (TPN) are not covered by the conditions of this policy.

4.2 Young people

As a child progresses through the teenage years there is a transitional stage of physical development i.e. adolescence, as that child progresses through towards adulthood. They will be referred to as 'young people' and many are cared for in adult wards by staff who generally treat adults.

The DHSSPSNI indicates that this paediatric fluid therapy guidance relates to all children from 1 month until their 16th birthday, regardless of the ward setting, except in the ICU and specialist areas mentioned above.

5. Objectives:

This policy sets out recommended practice for everyone who looks after children receiving intravenous fluids. It is based on regional and national guidance, ongoing clinical audit, the published literature and is also aimed at specifically reducing the risk of hyponatraemia.

It should be considered alongside the guidance from the National Patient Safety Agency Patient Safety Alert 22[1], and the Regional Paediatric Fluid Therapy Group wallchart[2] and the RQIA recommendations[5].

6. Roles and Responsibilities:

All professionals caring for children must:-

- be familiar with the signs of hyponatraemia.
- be familiar with its emergency management.
- ensure that they have received adequate training in intravenous fluids appropriate to their role.
- if they exclusively care for young people in an adult ward, know where to obtain expert paediatric should it be needed. (Appendix 5).
- be familiar with the guidance on intravenous fluids for children outlined by the Regional Paediatric Fluid Therapy Group wallchart[2].

7. The definition and background of the policy:

A child, for the purposes of this policy, is defined as being aged from 1 month up to their 16th birthday.

Hyponatraemia is an abnormally low concentration of sodium (Na) in serum. The normal range is generally agreed to be 135 – 145 mmol/L.

Hyponatraemia is defined as a plasma Na of less than 135 mmol/L. It represents an excess of water in relation to sodium in extracellular fluid and is described as severe or significant if below 130 mmol/L.

Significant acute hyponatraemia is defined as a decrease in plasma sodium from normal to less than 130 mmol/L in less than 48 hours.

Symptoms are likely with serum Na <125 mmol/L or if the serum Na has fallen rapidly; greater than 5 mmol/L decline in 24 hours.

The main causes of hyponatraemia in children are:

- Administration of hypotonic fluids, intravenous or enteral (e.g. excessively dilute formula or sodium chloride 0.18% and glucose 4% (No 18 solution))
- Conditions with impaired free water excretion and high anti-diuretic hormone levels
  - Meningitis, encephalitis, pneumonia, bronchiolitis, sepsis
  - Surgery, pain, nausea and vomiting
- Gastrointestinal fluid losses

Less common but important causes are:

- Adrenal insufficiency (Congenital Adrenal Hyperplasia, Addison's Disease)
- Defect in renal tubular absorption, including obstructive uropathy
- Psychogenic polydipsia

The main symptoms of hyponatraemia relate to its central nervous system effects; cerebral oedema, seizures and death. Warning signs may be non-specific and include nausea, malaise and headache.

All children are potentially at risk, even those not considered to be obviously 'sick'. The complications of hyponatraemia often occur because of the inappropriate management of intravenous fluids but they can also occur with inappropriately managed oral fluid regimes. Vigilance is required for all children receiving fluids.

Children particularly at risk are those who are postoperative, have gastrointestinal fluid losses or who have bronchiolitis, CNS injuries or burns. These risk factors also apply to young people.

8. Policy / Guideline description:

The NPSA recommended in Alert 22 the following actions:-

1. **Remove 'No. 18 solution'** from general areas that treat children and restrict availability to specialist areas except in critical care and specialist wards such as renal, liver and cardiac units.
2. Produce and disseminate **clinical guidelines** for the fluid management of paediatric patients.
3. Provide adequate **training** and supervision for all staff involved in the prescribing, administering and monitoring of intravenous infusions for children.
4. Review and improve the design of existing intravenous fluid prescriptions and **fluid balance charts** for children.
5. Promote reporting of hospital acquired hyponatraemia **incidents** via local risk management reporting systems. Implement an **audit** programme to ensure adherence to the above.

The 16 RQIA recommendations (appendix 7) map to the above NPSA recommendations:-

NPSA	RQIA
1	1, 2
2	3, (4), 5, 7
3	6, 7, 8, 9, 10
4	11
5	12, 13, 14,
6	15, 16

The specific actions that the BHSCT will institute in order to limit the production of hospital acquired hyponatraemia are detailed below and are mapped to the RQIA recommendations.

8.1.1 *Remove 'No. 18 Solution'*
NPSA 1 RQIA 1
Sodium chloride 0.18% with glucose 4% has been withdrawn from general use in all BHSCT ward areas that treat children and the availability of these fluids is restricted to critical care areas and other specialist wards such as renal, liver and cardiac units. A table showing areas permitted to stock or order 'No.18 solution' is given in Appendix 6.

8.1.2 *NPSA 1 RQIA 2*
Any area that is still permitted to stock 'No. 18 solution will arrange for the provision of additional labelling or separate storage.

8.1.3 *NPSA 2 RQIA 5*
Information about the availability of infusion fluids throughput the BHSCT (Appendix 4) will be attached to the Paediatric Fluid Guideline wall chart[2].

8.1.4 The BHSCT's list of sanctioned standard maintenance fluids is given in Appendix 4.

Where a senior clinician(s) considers that a "special" maintenance infusion fluid is required, then this alternative choice for fluid maintenance must be endorsed by the Chief Executive of the Trust with clear documentation of the reasons for that endorsement.

8.2 *Clinical Guideline*
NPSA 2 RQIA 3,5,7
The Paediatric Parenteral Fluid Therapy wallchart[2] forms the basis of BHSCT guidance on fluid prescription in paediatric patients within the previously defined age range. This policy and wall chart will be disseminated and displayed throughout the BHSCT; to all wards that accommodate children aged from one month until their 16th Birthday including Emergency Departments, Adult Wards, Theatre and Intensive Care Units.

This will replace any previous wallchart including the 2002 wallchart issued by CMO entitled "Any Child Receiving Prescribed Fluids is at Risk of Hyponatraemia". All previous versions of the chart should be removed.

8.2.1 *NPSA 2 RQIA 7*
The BHSCT will develop policy and guidelines on the general principles of intravenous therapy for adults and children.

Until then, this policy will form the basis of guidance on fluid therapy in children within the BHSCT and, as for all BHSCT policies, it will be reviewed and implemented throughout the organisation.

8.2.3 *NPSA 2 RQIA 3*
All medical and nursing staff should base their intravenous fluid practice for children, young people (and indeed adults) on the following best practice model of:-

- administer appropriate therapy for shock such as fluid boluses
- measure/estimate and correct any fluid deficit
- prescribe a fluid maintenance fluid regime.

Treatment of these elements of the overall fluid status is outlined in the Paediatric Parenteral Fluid Therapy wallchart[2].

The fundamental layout selected for this guideline complements a structured approach to patient clinical assessment. A sequence of questions is offered that prompts the clinician to

- assess for the presence of shock and guides treatment, if required;
- further assessment of whether there is also a deficit to be considered and then
- calculation and prescribing for maintenance requirements is also included.

8.2.4 This policy, centred on children, has many features that indicate good practice for young people and adults. An intravenous fluid therapy practice based on using

- an individual patient's weight in kilograms
- fluid administration based on a millilitres/hour prescription

is commended rather than blanket prescriptions based only on fluid volume.

8.2.5 Baseline Assessment

Good practice guidelines on monitoring body weight, electrolytes/urea and fluid balance should be followed. Again, these recommendations apply to adults as well as children.

An essential preliminary to these assessments is to accurately measure the body weight in kilograms or failing this, to make an estimate. This must be cross-referenced with the child's age to minimize the risk of error.

In the emergency situation an estimation of the child's weight should be made and an accurate weight obtained as soon as practically possible.

Baseline measurement of electrolytes and urea should be made unless the child is healthy and scheduled for elective surgery when it may be considered unnecessary.

8.2.6 Shock therapy

Shocked or collapsed children must immediately receive fluid boluses as outlined on the Regional Paediatric Fluid Therapy Group wallchart[2].

Good practice would indicate that the response to fluid therapy is closely observed and if there is no response by the time 40 mls/kg has been administered, senior medical advice and help is required.

Note that special treatment is needed for children with diabetic coma and trauma and the need to obtain senior advice and help is highlighted.

8.2.7 Fluid Deficit management

Calculation of the overall fluid deficit and the prescription of deficit replacement should only be undertaken by a doctor experienced in caring for dehydrated patients. The recommended fluid is sodium chloride 0.9% and it must be prescribed separately. The rate at which it is given is determined by the degree of dehydration and a relevant electrolyte sample.

For those caring for young people in a general adult ward, and who may not have such experience, they should ensure that they can avail themselves of advice from the sources as detailed in Appendix 5.

8.2.8 For advice regarding the estimation of the percentage of dehydration which is required for the fluid deficit calculation, the table in Appendix 2 should be consulted.

8.2.9 Maintenance fluid therapy
When prescribing maintenance fluids to children, young people and adults, the following scheme would be standard practice. For

- children use the calculations as indicated in the Regional Paediatric Fluid Therapy Group wallchart[2].
- young people and adults prescribe
    - 2 litres fluid for females over the weight of 40 kg.
    - 2.5 litres fluid for males over the weight of 60 kg.

8.2.10 The type of fluid selected must be tailored to the patient's needs as set out in the guideline. For example, following surgery, children who require intravenous fluids will be prescribed either sodium chloride 0.9% with or without pre-added glucose or Hartmann's solution in the post-operative period for maintenance fluid needs.

8.2.11 Children must not receive intravenous fluids unnecessarily. This guideline emphasises that assessment of each patient should include a decision on whether oral fluid therapy could be appropriately initiated instead of intravenous therapy and further prompts reconsideration of this question when IV therapy is reviewed.

8.2.12 This advice does not override or replace the individual responsibility of health professionals to make appropriate decisions in the circumstances of their individual patients, in consultation with the patient and/or guardian or carer or for consultation with a more senior clinician. This would, for example, include situations where individual patients have other conditions or complications that need to be taken into account in determining whether the guidance as detailed in the wallchart[4] is fully appropriate in their case.

8.3 Training
NPSA 3 RQIA 3,6,8,10
The BHSCT will use various forms of training on paediatric fluid management; didactic lectures, staff induction training and computer based training:-

1. a training presentation in the policies and guidelines section of the Intranet. This multidisciplinary presentation is accessible from any computer terminal within the BHSCT.
2. BMJ e-learning module
3. 'Training Tracker' (Multimedia Design Studio Limited).

The BHSCT advocates the adoption of a regional computer based educational tool that allows:-

- creation of an unlimited number of educational and training courses; to include mandatory modules.
- 'training' of all grades of staff.
- content of the training to be tailored to our own needs.
- tracking
    - who has taken each module.
    - who has not taken each module.
    - who has passed and who has failed.
    - precisely which questions each trainee got right and wrong.
- competency assessment tools.
- training record to be obtained at any time.
- to award personalised certificates to those who reach a stated passmark.

8.3.1 *NPSA 3 RQIA 6,8,10* All staff involved in prescribing, administering and monitoring IV fluids to children will be made aware of this policy and the Paediatric Parenteral Fluid Therapy wallchart[2] through the BHSCT intranet and Service Group dissemination.

All staff working exclusively with children and especially those prescribing fluids to children will be encouraged to ensure they are conversant with the knowledge required to prescribe intravenous fluids to children and that it is within their scope of practice.

They will be encouraged to use the intranet training presentation and the BMJ learning module on hyponatraemia - http://learning.bmj.com/learning/search-result.html?moduleId=5003358

The production of the certificate on completion of the above module may be sought at staff assessments, RITAs, performance review, personal development plans and appraisals.

The future BHSCT policy and guideline on the general principles of intravenous therapy (8.2.1) will also be available in the various training modules.

8.3.2 *NPSA 3 RQIA 6,8* All professionals caring for children must be familiar with the signs of hyponatraemia and its emergency management.

8.3.3 *NPSA 3 RQIA 6,8* For those caring for young people, they should either have received adequate training in intravenous fluids or if they exclusively care for young people in an adult ward, they should know where to obtain such expertise on children should it be needed. (Appendix 5).

Furthermore, they should be familiar with the guidance on intravenous fluids for children outlined in this policy and Regional Paediatric Fluid Therapy Group wallchart[2].

8.3.4 *NPSA 3 RQIA 9* The BHSCT has identified that young people aged 14 - 16 years old can be cared for (even if only occasionally) on most wards that are generally regarded as adult wards with the obvious exceptions of wards like Care of the Elderly. Staff in those locations will be made aware of the training opportunities mentioned in 8.3 and 8.3.1.

BHSCT Service groups will consider cohorting young people in dedicated wards - where this can be done safely and will not lead to any diminution in the level of care.

8.3.5 The BHSCT will work with the NIMDTA to ensure that the principles of paediatric fluid therapy and its potential risks, as highlighted in the National Patient Safety Agency Alert, are highlighted in postgraduate training programmes.

8.3.6 All professionals caring for children must be able to diagnose and manage acute hypoglycaemia.

8.4 *NPSA 4 RQIA 11* Fluid prescription/ balance chart

A new fluid prescription/ balance chart has been developed within the Royal Belfast Hospital for Sick Children (RBHSC) with guidance from all other areas in the BHSCT that treat children. It will be used for the prescription of fluids for all children and young people treated in the BHSCT with the exception of treatment of diabetic ketoacidosis (DKA) when a specialised fluid prescription chart may be used.

If needed, they should avail themselves of advice from the sources as detailed in Appendix 5.

8.4.1 All children, other than emergencies, must have a blood sample taken for electrolyte and blood glucose estimation before intravenous maintenance fluids are started. This must be repeated at least 24 hourly, more often in the circumstances described. Clinical and other methods of monitoring are outlined in the guidance.

8.4.2 Monitoring

Monitoring of the child receiving parenteral fluid will include considerations of:-

- Body weight to be measured or assessed as a baseline and at least daily thereafter.
- Clinical state to be closely monitored and recorded on a regular basis.
- All fluid intake of any kind (intravenous, oral and medicines) must be measured and recorded on the fluid balance chart.
- All fluid output must be assessed and, if clinically indicated, measured and recorded on the fluid balance chart.
- An assessment of input/output and need for plasma glucose estimation should be made and documented every 12 hours.
- A formal reassessment of the fluid prescription and the need for intravenous fluids must be made and documented every 12 hours.
- Measurement of E&U and blood glucose/BM should be made at least daily.
- If hyponatraemia exists, these measurements should be 4 – 6 hourly.
- Urinary osmolarity and electrolytes measurements should be considered when dealing with hyponatraemia.
- The ill child will require more frequent and detailed investigations.

For more detailed information about the monitoring requirements the wallchart[2] should be consulted.

8.5 **Audit**

NPSA 5 RQIA 12 The BHSCT will implement the following governance measures.

8.5.1 *NPSA 5 RQIA 13* The BHSCT clinical biochemistry department will collate, analyse and report quarterly on paediatric hyponatraemia incidents to designated clinicians for children and young people. They will regularly audit these incidents, collate them with the Trust Adverse Incident Reporting System and instigate actions linked to the NPSA Alert 22. Appendix 3 outlines this audit process.

8.5.2 Incident reporting

NPSA 5 RQIA 14 The BHSCT will report these potential adverse incidents related to intravenous infusion through the Trust Adverse Incident Reporting System.

A system of 'triggers' (adapted from those developed by the NHSCT) will be used to

- generate a list of hospital acquired hyponatraemia episodes
- highlight variance from best practice guidance as highlighted in this document
- generate a Trust Adverse Incident Form whenever such incidents occur.

These triggers (Appendix 3) will cover the choice of fluid prescribed at ward level, charting relevant findings in the medical notes, the frequency of electrolyte analysis and the detection of biochemical abnormalities.

8.5.3 Audit

NPSA 5 RQIA 15,16 The BHSCT will implement an audit programme for intravenous infusion therapy in children throughout the trust.

The audits will be based on the

- NPSA audit checklist
  http://www.npsa.nhs.uk/EasySiteWeb/GatewayLink.aspx?alId=5308
- the BHSCT trigger list (Appendix 3).
- Regional GAIN hyponatraemia audit

8.5.4 Where young people are cared for in general adult wards, special audit arrangements will be put in place to ensure they receive appropriate and safe fluid management.

9. Additional policy statements:

9.1 Senior medical advice must be sought when treating the child with hyponatraemia.

9.2 Where additional electrolytes are required, they should only be administered as supplied by the manufacturer and in line with guidance.

Children at or below the age of 13 years must not have electrolytes added to bags of intravenous fluids.

Ordinarily children from 13 to 16 should also not have electrolytes added to bags of intravenous fluids; in certain, predominantly adult areas, children of this age group may have magnesium sulphate or phosphates added.

9.3 Apart from boluses for shocked patients, fluids may only be administered by way of an infusion device. Details of the pump must be recorded on the fluid prescription and balance chart.

9.4 When referring to this policy, staff should consult the BHSCT policy on the management of strong intravenous potassium solutions and/or injections.

10. Implementation / Resource requirements:

The implementation requirements for this policy include:-

- Wallchart production and distribution
- Fluid prescription/ balance chart production and distribution
- Staff training costs – induction, postgraduate courses.

Raising staff awareness of the issues surrounding hyponatraemia and the subsequent staff training will be encouraged, as suggested by DHSSPSNI circular[4], by using the BMJ e-learning module.

11. Source(s) / Evidence Base:

The following sources were used:-

a) NPSA Alert 22
b) NPSA background information
   http://www.npsa.nhs.uk/EasySiteWeb/GatewayLink.aspx?alId=5310
c) HSC (SQSD) 20-07 - reducing risk of Hyponatraemia in children (27/04/2007)
d) HSC (SQSD) 20-07 - addendum (16/10/2007)
e) Paediatric Parenteral Fluid Therapy wallchart.

12. References, including relevant external guidelines:

1. Reducing the risk of hyponatraemia when administering intravenous infusions to children. National Patient Safety Agency, Patient Safety Alert 22, March 2007.
2. Paediatric Parenteral Fluid Therapy initial management guideline, DHSSPSNI 2007. http://www.dhsspsni.gov.uk/hsc_sqsd_20-07_wallchart.pdf.
3. HSC (SQSD) 20-07 reducing risk of Hyponatraemia in children
4. http://www.dhsspsni.gov.uk/hsc_sqsd_20-07_-_addendum.pdf

5. Regulation and Quality Improvement Authority (RQIA). Reducing the risk of hyponatraemia when administering intravenous infusions to children - September 2008. http://www.rqia.org.uk/cms_resources/NI%20%20report%20Hyponatraemia%20FINAL%20v%203%200.pdf

13. Consultation Process:

This policy is adapted from the

- NPSA Alert 22,
- Northern Ireland Regional Paediatric Fluid Therapy Working Group
- HSC (SQS) 20/2007 and its addendum documentation from the DHSSPSNI.

It has been assured through the Standards and Guidelines committee.

14. Equality and Human Rights screening carried out:

In line with duties under the equality legislation (Section 75 of the Northern Ireland Act 1998), Targeting Social Need Initiative, Disability discrimination and the Human Rights Act 1998, the Belfast Trust has carried out an initial screening exercise to ascertain if this policy should be subject to a full impact assessment.

√ Screening completed ☐ Full impact assessment to be carried out.
No action required.

15. Procedures:

Appendix 1 - Paediatric Parenteral Fluid Therapy wallchart
Appendix 2 - Estimating the percentage dehydration based upon physical examination findings.
Appendix 3 - Paediatric Hospital Acquired Hyponatraemia Audit
- Triggers for potential adverse events
Appendix 4 - Availability of intravenous fluids throughout the BHSCT (500ml bags)
Appendix 5 - Sources of advice regarding Paediatric fluid therapy
Appendix 6 - Areas where it is permitted to stock/order No. 18 Solution* - as of August 2009
Appendix 7 - RQIA independent review - September 2008 - Recommendations

Director **Author**

Date: **Date:**

PAEDIATRIC PARENTERAL FLUID THERAPY (1 month – 16 yrs)

Initial management guideline

Sept 2007

Monitoring & observations essential

ALL CHILDREN

Admission Weight. U&E *(unless child is well & for elective surgery)*

12 Hourly –
Assess In / Output, plasma glucose

Daily – Clinical reassessment. U&E (more often if abnormal; 4-6 hourly if Na^+ < 130 mmol/L).

ILL CHILDREN
May need:
Hourly - HR, RR, BP, GCS. Fluid In/ Output (urine osmolarity if volume cannot be assessed)
2-4 hourly – glucose, U&E, +/- blood gas.

Daily – weight if possible

Each shift
Handover and review of fluid management plan.

If plasma Na^+ < 130 mmol/L or > 160 mmol/L or plasma Na^+ changes > 5 mmol/L in 24 hours ask for senior advice

Is shock present? — YES →

ADMINISTER RAPID FLUID BOLUS
Give 20 ml/kg sodium chloride 0.9% IV or Intraosseous
[10 ml/kg if history of haemorrhage or in diabetic ketoacidosis]
Reassess. Repeat bolus if needed. Call for senior help.
(Up to 60 ml/kg may be needed. Use blood after 40 ml/kg if patient has haemorrhaged)

NO ↓

Can child be managed with oral fluids? — YES →

PRESCRIBE ORAL REHYDRATION SOLUTION

DKA / burns: initiate departmental protocol. Renal / cardiac / hepatic - get senior advice.

Is there a fluid deficit? — YES →

ESTIMATE DEFICIT
FLUID DEFICIT = (% dehydration x kg x 10) as mls of:
sodium chloride 0.9%

The volume of fluid to be prescribed is: fluid deficit MINUS volume of any fluid bolus received

Prescribe this residual volume of deficit separately from the maintenance prescription.
Give over 24 hours (but over 48 hours if Na^+ < 135 or > 145 mmol/L)

ONGOING LOSSES: calculate at least 4 hourly. Replace with an equal volume of:
sodium chloride 0.9% (with or without pre-added potassium)

Be prepared to change fluid type and volume according to clinical reassessment, electrolyte losses and test results

NO ↓

Prescribe Maintenance fluids →

PRESCRIBE INITIAL IV MAINTENANCE FLUID AND TIME FOR REASSESSMENT

Patients particularly at risk of hyponatraemic complications:
peri-operative patients; patients with head injuries; gastric losses; CNS infection; severe sepsis; hypotension; intravascular volume depletion; bronchiolitis; gastroenteritis with dehydration; abnormal plasma sodium, particularly if less than 138 mmol/L but also when greater than 160 mmol/L; salt wasting syndromes.

Fluid choices: glucose containing fluid normally required if under 1 year old and may also be required by older children

sodium chloride 0.9% (with/ without pre-added glucose 5%)
or
Hartmann's Solution
or
Solution Corporately Approved at Trust Level

Other Patients:
sodium chloride 0.45% with pre-added glucose 2.5% or 5%

All Patients:
Alter fluid rate according to clinical assessment. Change electrolyte and glucose content of infusion fluid according to test results.
COMMENCE ORAL FLUIDS & DISCONTINUE IV FLUIDS AS SOON AS POSSIBLE

CALCULATION OF 100% MAINTENANCE RATE

(a) for first 10 kg:	100 ml/kg/ day	≡ 4ml/kg/hr
(b) for second 10 kg:	50 ml/kg/ day	≡ 2ml/kg/hr
(c) for each kg over 20 kg:	20 ml/kg/ day	≡ 1ml/kg/hr

[for 100% daily maintenance add together (a) + (b) + (c)]

MAXIMUM: in females 80 mls per hour; in males 100 mls per hour
If risk of hyponatraemia is high consider initially reducing maintenance volume to two thirds of maintenance

Hypokalaemia (< 3.5 mmol/L): Check for initial deficit. Maintenance up to 40 mmol/L IV potassium usually needed after 24 hrs using pre-prepared potassium infusions as far as possible. Consult Trust Policy on IV strong potassium.
Oral intake and Medications: volumes of intake, medications & drug infusions must be considered in the fluid prescription.
Hypoglycaemia (< 3 mmol/L). Medical Emergency: give 5 ml/kg bolus of glucose 10%. Review maintenance fluid, consult with senior and recheck level after 15-30 mins. **INTRA-OPERATIVE PATIENTS:** consider monitoring plasma glucose.
Symptomatic Hyponatraemia: check U&E if patient developes nausea, vomiting, headache, irritability, altered level of consciousness, seizures or apnoea. This is a Medical Emergency and must be corrected.
Commence infusion of sodium chloride 2.7% at 2 ml/kg/hour initially and get senior advice immediately.

Appendix 2

Estimating the percentage dehydration based upon physical examination findings.

Estimated Percentage Dehydration	Physical Examination Findings
<3	History of fluid loss but no findings on physical examination
5	Dry oral mucous membranes but no panting or pathological tachycardia
7	Mild to moderate decreased skin turgor, dry oral mucous membranes, slight tachycardia, and normal pulse pressure.
10	Moderate to marked degree of decreased skin turgor, dry oral mucous membranes, tachycardia, and decreased pulse pressure.
12	Marked loss of skin turgor, dry oral mucous membranes, and significant signs of shock, pallor, cool peripheries, prolonged capillary refill time, hypotension, confusion.

Appendix 3

PAEDIATRIC HOSPITAL ACQUIRED HYPONATRAEMIA AUDIT

Laboratory Report Details (to be completed by audit dept)

Patient No. Patient Date of Birth:

Date of specimen: Time of specimen: Result :

Admission Details

Date of admission: Time of admission:

Diagnosis: 1.

2.

Hospital acquired hyponatramia (defn)

- Na ≥130mmol/l at time of admission, & a subsequent Na of < 130mmol/l whilst on IV fluids.
- Na< 130mmol/l on their initial U&E's, where the U&E's are done >48hrs after admission and they are on IV fluids.
- Admitted from another hospital with Na < 130mmol/l at time of admission whilst on IV fluids.

1. Is this hospital acquired hyponatraemia? Yes / No

   If no, reason: _____

   If yes, was it acquired whilst in this trust? Yes / No

   If no, patient transferred from: _____

Treatment and monitoring of hyponatraemia

2. Was the fluid prescribed appropriate? Yes / No

   If no, details: _____

3. Was IV fluid prescription reviewed 12hrly whilst on IV fluids? Yes / No

4. Were U&E done 24hrly whilst on IV fluids? Yes / No

Following the Na of <130mmol/l,

5. Was appropriate advice sought? Yes / No

   Grade: _____ Speciality: _____

6. Was the frequency of repeat U&Es appropriate? Yes / No

   If No, details: _____

Recording and communication of incidents (to be completed by Audit dept)

7. If yes to Q1, was adverse incident form completed? Yes / No

8. Was copy of form sent to other trust if acquired outside BHSCT? Yes / No

Triggers for potential adverse events related to the administration of intravenous fluids to children (1 month – 16 years old)

(adapted from Northern H&SCT policy)

CHOICE OF IV FLUID

1. Bolus fluid: use of a solution with sodium concentration of <131mmol/L for treatment of shock.
2. Deficit fluid: use of a solution with sodium concentration of <131mmol/L for correction.
3. Maintenance fluid: use of a solution with sodium concentration of <131mmol/L in a peri-operative patient (intraoperative period and first 24 hours following surgery).

BIOCHEMICAL ABNORMALITIES

4. Any episode of symptomatic hyponatraemia while in receipt of IV fluids.
5. Any episode of hypoglycaemia (blood glucose less than 3mmol/L) while in receipt of IV fluids.
6. Any episode of severe acute hyponatraemia (i.e. sodium level dropping from 135mmol/L or above to < 130mmol/L within 24hrs of starting IV treatment).

ASSESSMENT

7. Electrolytes not checked at least once per 24 hours in any patient receiving IV fluids exclusively.
8. Failure to record the calculations for fluid requirements on the prescription sheet.
9. Failure to note in the case notes/ prescription sheet a serum sodium of less than 130mmol/L.
10. Failure to document in the case notes the steps taken to correct a serum sodium of less than 130mmol/L.

If any of the above occurs an IR1 Form must be completed.

October 2010

Appendix 4

AVAILABILITY OF INTRAVENOUS FLUIDS THROUGHOUT THE BHSCT (500ML BAGS)

SITE	RGH	BCH	MPH	MATER
Sodium chloride				
Sodium chloride 0.45%	√	√		√
Sodium chloride 0.9%	√	√	√	√
Sodium chloride 1.8%	√	√	√	√
Sodium chloride 2.7%	√		√	√
Combined solutions				
Sodium chloride 0.45% Glucose 2.5%	√	√	√	
Sodium chloride 0.45% Glucose 5%	√		√	
Sodium chloride 0.9% Glucose 5%	√			
Glucose solutions				
Glucose 5%	√	√	√	√
Glucose 10%	√	√	√	√
Glucose 15%	√			
Glucose 20%	√	√		
Potassium containing solutions				
Glucose 5% 10mmol Potassium chloride	√			
Glucose 5% 20mmol Potassium chloride	√	√	√	
Glucose 5% 40mmol Potassium chloride	√	√	√	
Glucose 10% 10mmol Potassium chloride	√			√
Glucose 10% Sodium chloride 0.18% 10mmol Potassium chloride*	√			
Sodium chloride 0.45% Glucose 2.5% 10mmol Potassium chloride	√	√		
Sodium chloride 0.45% Glucose 2.5% 20mmol Potassium chloride	√			
Sodium chloride 0.45% Glucose 5% 10mmol Potassium chloride	√			
Sodium chloride 0.45% Glucose 5% 20mmol Potassium chloride	√			
Sodium chloride 0.9% 10mmol Potassium chloride	√			
Sodium chloride 0.9% 20mmol potassium chloride	√	√	√	√
Sodium chloride 0.9% 40mmol potassium chloride	√	√		

* commonly known as Basic solution

Sites: RGH = Royal Hospitals
BCH = Belfast City Hospital
MPH = Musgrave Park Hospital
MATER = Mater Hospital

Appendix 5

Sources of advice regarding Paediatric fluid therapy

For help and advice regarding

- management of fluid therapy
- especially to prevent and/or treat hyponatraemia

in all children, but especially for those children aged 13 – 16 years old being managed in adult wards,

please use the following sources of help and advice. Ordinarily, advice should be for complex cases and should be Consultant to Consultant discussions even though contact will often have to be made through trainee on-call rotas.

Team		Address	Extension
RBHSC Paediatricians	Paediatric On Call Rota	Allen Ward Musgrave Ward	Bleep 2277
RBHSC Paediatric ICU	Paediatric ICU		2449
Musgrave Park	Orthopaedic theatre – Anaesthesia team during working hours.		
BCH Dufferin theatres	ENT theatre – Anaesthesia team during working hours.		
General Biochemistry	**Clinical Biochemistry**		
	Inside working hours	**Outside working hours**	
RVH Tie line:7222 Ext.3798	Ext.4714	Contact Medical doctor on call either via the laboratory or via switchboard.	
BCH Tie line:7111 Ext. 3096/2926/3628	Ext.3497/3136/3160	Ext.3216 or Contact Medical doctor on call either via the laboratory or via switchboard	
MIH Tie line: 7231 Ext. 2223/2229	Ext.2326/2228	Contact Medical doctor on call either via the laboratory or via switchboard	

Other sources of help are:

1 APA consensus guideline on perioperative fluid management in Children
http://www.apagbi.org.uk/docs/Perioperative_Fluid_Management_2007.pdf

2 Royal Children's hospital Melbourne Clinical Practice Guidelines
Intravenous fluids
http://www.rch.org.au/clinicalguide/cpg.cfm?doc_id=5203#Other%20Resources

3 Royal Children's hospital Melbourne Clinical Practice Guidelines
Hyponatraemia
http://www.rch.org.au/clinicalguide/cpg.cfm?doc_id=8348

Appendix 6

Areas where it is permitted to stock/order No. 18 Solution* - as of August 2009

SERVICE GROUP	SITE	SPECIALITY	Stock on Ward	Named patient supply – consultant request only.
Clinical Services	RGH, BCH	High Dependency Unit	X	
Clinical Services	RGH, BCH, MATER	Intensive Care	X	
Clinical Services	Mater, BCH, RGH	Recovery Wards		X
Clinical Services	Mater, RGH	Theatres		X
Clinical Services	BCH	Tower Theatres		X
Clinical Services / OPMS	Mater, RGH, BCH	Day Procedure Units		X
Specialist Serv	RGH	Wards 4E and 4F (Neurosciences)		X
OPMS T&O	MPH	Recovery Ward - Orthopaedics		X
OPMS T&O	MPH	High Dependency Unit		X
OPMS T&O	MPH	Theatres - Orthopaedics		X
SS, Women, family and childcare	RBHSC	Barbour Renal	X	
SS, Women, family and childcare	RBHSC	PICU	X	

* "No. 18 Solution" = sodium chloride 0.18% and glucose 4%

Appendix 7

RQIA INDEPENDENT REVIEW - SEPTEMBER 2008 - RECOMMENDATIONS

Recommendation 1	All hospitals should monitor the ongoing use of No. 18 solution to enable assurance that infusions are removed from stock and general use in areas that treat children.
Recommendation 2	Where appropriate, hospitals must be able to demonstrate that an active strategy is in place for minimising risk of use in clinical areas that continue to stock No 18 solution and where children are accommodated. For example, provision of additional labelling or separate storage for those No.18 solution bags still stocked in such clinical areas.
Recommendation 3	All hospitals should continue with the ongoing work of disseminating clinical guidelines. This should be undertaken in conjunction with multidisciplinary awareness-raising and education on the use of the guidance and wall chart in all settings where children may be treated. This is particularly important in adult wards where older children are treated.
Recommendation 4	Independent hospitals must be assured that all visiting doctors who may manage patients up to 16 years old use the clinical guidelines when managing children being treated with intravenous infusions.
Recommendation 5	All hospitals should ensure that only the DHSSPS Paediatric Parenteral Fluid Therapy wall-chart *issued by DHSSPS in October 2007* is displayed in clinical areas where children may be treated, with a list of available local fluids available alongside it. All previous versions of the wall chart should be removed from clinical areas.
Recommendation 6	Hospitals should assure themselves that staff have the appropriate skill and knowledge in this clinical area. Competency assessment tools in administration of intravenous infusion to children should be developed, formalised and implemented for all relevant, multi-professional staff.
Recommendation 7	Hospitals should continue to review, collaborate and implement organisation wide policy and guidelines, in relation to intravenous infusion for children.
Recommendation 8	All hospitals should ensure that the development and provision of multidisciplinary education opportunities in administration of intravenous infusion to children and that all relevant clinical staff uptake this education.
Recommendation 9	Hospitals should develop mechanisms to identify the location of patients aged 14-16 years who are in adult wards and ensure staff who care for those children are provided with competency based, assessed education in administration of intravenous infusion to children.
Recommendation 10	All hospitals should make wider use of training sources available such as BMJ E-Learning Module on Hyponatraemia to address different learning styles and devise a mechanism to ensure 100% multi-professional uptake of such learning.
Recommendation 11	Priority must be given to the completion of a Trust-wide review, and implementation of revised paediatric intravenous fluid prescription and

fluid balance charts in all settings where children may be treated including adult wards where children are treated.

Recommendation 12 All hospitals should develop a culture of incident reporting, analysis and learning generally and specifically in respect of intravenous fluids and hyponatraemia.

Recommendation 13 Plans for development of systems for reporting, analysing and monitoring incidents to assure organisations of safe practice and that actions linked to NPSA Alert 22 should be implemented and regularly audited by all hospitals to ensure adherence to the process.

Recommendation 14 The development of 'trigger lists' that have been adopted by a the Antrim Area Hospital to aid understanding of the types of incidents to be reported should be shared and taken up more widely .

Recommendation 15 The development of an audit tool which may include wider aspects but should address as a minimum aspects of NPSA Alert 22 should continue to be progressed and used at least annually.

Recommendation 16 Trusts should continue to seek approval and funding for a regional audit (GAIN proposal) on the uptake of the Paediatric Parenteral Fluid Therapy guideline and potential unexpected clinical consequences of the guideline.

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Paediatric renal transplantation in Northern Ireland (1984-1998)

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Accepted 5 May 2000

SUMMARY

Over the last 20 years a comprehensive paediatric nephrology service has been developed in Northern Ireland, based in the academic medical unit at the Royal Belfast Hospital for Sick Children (RBHSC). In the 15 years 1984-1998 a total of 77 renal transplants have taken place in patients aged 18 years and under. Initially transplants were only considered in children over five years of age but in the past eight years children as young as two years have successfully received kidneys. Aggressive nutritional support combined with peritoneal dialysis has enabled survival to a size when transplantation is feasible. The 5 year graft survival was 64%, with two children dying following transplantation. The complexity of managing this age group is reflected by the fact that a total of 10 transplants (13%) failed in the first 30 days. These figures compare favourably with statistics reported by similar paediatric centres from across the United Kingdom and Republic of Ireland, and with local results in adult patients. This demonstrates that a successful end stage renal replacement programme for children is achievable in a relatively small population, which is geographically isolated.

INTRODUCTION

Paediatric renal transplantation began in Northern Ireland in 1980. Despite clinical experience being limited by a relatively small population, long term graft and patient survival rates are comparable to other centres throughout the UK and Republic of Ireland. This represents a beneficial initial sharing of adult nephrology expertise with the paediatric team, and subsequent development of the ability to manage independently even the smallest child with renal failure.

METHODS AND PATIENTS

Data was provided by the United Kingdom Transplant Support Service Authority from the national transplant database. All patients 18 years and under at the time of renal transplantation in Northern Ireland between the years 1984 and 1998 inclusive were included. Information was collected relating to primary diagnosis, donor and recipient age, waiting time on the transplant list, organ refusal, graft and patient survival, cause of graft loss and growth parameters post transplant.

RESULTS

From 1984-1998 a total of 77 cadaveric renal transplants have taken place in Northern Ireland in patients 18 years of age and under. The commonest primary diagnosis was reflux nephropathy in 31 cases (40.3%), eight cases were caused by hereditary nephropathy (10.4%) and seven by glomerulonephritis (9%). Five (6.5%) cases were caused by congenital renal hypoplasia or dysplasia and one (1.3%) by each of the following – infantile polycystic kidney, medullary cystic disease, Alports disease and cystinosis. 22 cases were classified in the national transplant database as other diagnosis and not

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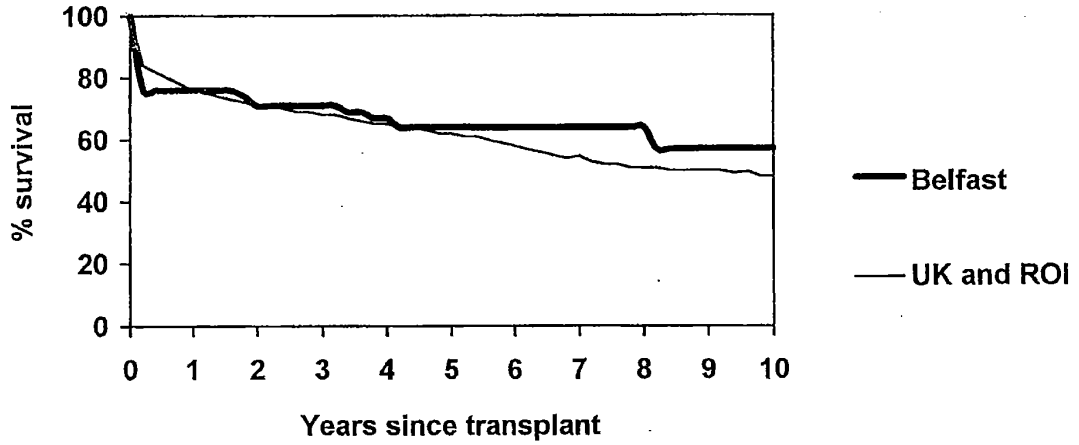

Fig 1. 10 year transplant survival plot for first cadaveric paediatric kidney grafts since 1984, Belfast v rest of UK and Republic of Ireland (ROI).

further specified. The five year graft survival was 64% (fig.1).

From 1984-1988 inclusive 15 donors (68% of donors for this 5 year period) to paediatric recipients were order then 18 years. In 1989-1993 10 donors (43% of donors for this 5 year period) and in 1994-1998 nine donors (28% of donors for this 5 year period) were adults. 23 donors in the period 1994-1998(72% of donors for this 5 year period) were 18 years or less with 17 (53%) in the 5-14 age group.

In the period 1984-1990 all recipients were older than 5 years of age. From 1990-1998 nine transplants took place in the age group 2-4 years, none have taken place in recipients less than 2 years of age.

In 1984-1988 twenty-two patients waited on the transplant waiting list for a median time of 87 days, in 1989-1993 twenty five waited for a median time of 182 days and from 1994-1998 thirty patients waited a median time of 316 days for transplant.

One hundred and seventeen offers of organs were refused from 1984-1998. The commonest reason in 66 cases (56%) was an inadequate tissue match. Eight offers (6.8%) were rejected because the recipient was unfit, and eight because of lack of resources; 18 (15.4%) were not used because of problems related to donor age, size or history. In four (3.4%) cases the ischaemic time was unfavourable, a further four had associated adverse clinical factors. One (0.8%) was rejected for an anatomical reason, a further eight for reasons unspecified in the National Database.

Of the 77 transplants seven failed in the first 7 days post transplant and an additional three during days 8 to 30 (13%). Two deaths occurred in the early postoperative period (mortality rate of 2.6%). The causes were fluid overload and ARDS (acute respiratory distress disorder).

Of the children currently attending the RBHSC transplant follow-up clinic the mean standard deviation score for height is -0.83, with a range of -2.3 to +1.4. Only two children have a standard deviation score of less than -2.

DISCUSSION

Interest in transplantation dates back for centuries but the earliest experiments that met with any success occurred in the first decade of the last century. Kidneys that functioned briefly are recorded after transplantation from one dog to another by Ullman in 1902. By the fourth and fifth decades of the 20th century attempts were being made to transplant a kidney from a cadaver to a live recipient, but invariably met with failure. A breakthrough occurred in 1954 in Boston when an identical twin donated a kidney to his sibling and the graft survived for 8 years, failing because of recurrence of the primary disease.[1]

In Belfast the first adult renal transplant which took place in 1962 between identical twins failed because of technical problems, but led to a successful haemodialysis and transplant programme for adults. A programme for children was inaugurated in 1980 with the appointment of a paediatric nephrologist and the introduction of a continuous peritoneal dialysis program using parent-operated automated cyclers. The service

is presently run by a multidisciplinary team led by 2 paediatric nephrologists (the second appointment being in 1995) supported by 3 renal nurse specialists, and a part time psychologist, dietician and social worker. All surgery is performed by renal transplant surgeons based at the Belfast City Hospital.

The United Kingdom Transplant Support Service Authority (UKTSSA) has recently published audit figures for renal transplants in the United Kingdom and Republic of Ireland for 1984-1993[2] and in this ten year period 1406 paediatric renal transplants (18 years and under) have taken place. Table I illustrates how Belfast compared with other centres on a numerical basis during this 10 year period.

In the 15 year period from 1984-1998 a total of 77 cadaveric renal transplants have taken place in Northern Ireland in patients under the age of 19 years. The 5 year graft survival of 64% compares favourably with nation-wide statistics (fig.1). 1990 was a particularly busy year (fig.2) when a total of 10 transplants took place supervised by a single paediatric nephrologist, with the active support of the adult nephrology team. The commonest primary diagnosis was reflux nephropathy, which explains the preoccupation of all paediatricians with the investigation of childhood urinary tract infections. There is the potential that some patients who present late in

TABLE I

Cadaveric kidney transplants in recipients aged 0-18 years at time of transplantation (1984-1993). (Population base ref. 14)

Hospital	*Number of Transplants*	*Population base (millions)*
Guys	238	9.13
Great Ormond Street/Royal Free	162	11.65
Manchester	132	4.0
Birmingham	117	5.49
Leeds	97	3.67
Dublin	83	4.5
Glasgow	79	5.1
Newcastle	65	3.03
Cardiff	58	2.16
Bristol	56	3.93
Belfast	47	1.59
Liverpool	26	3.06

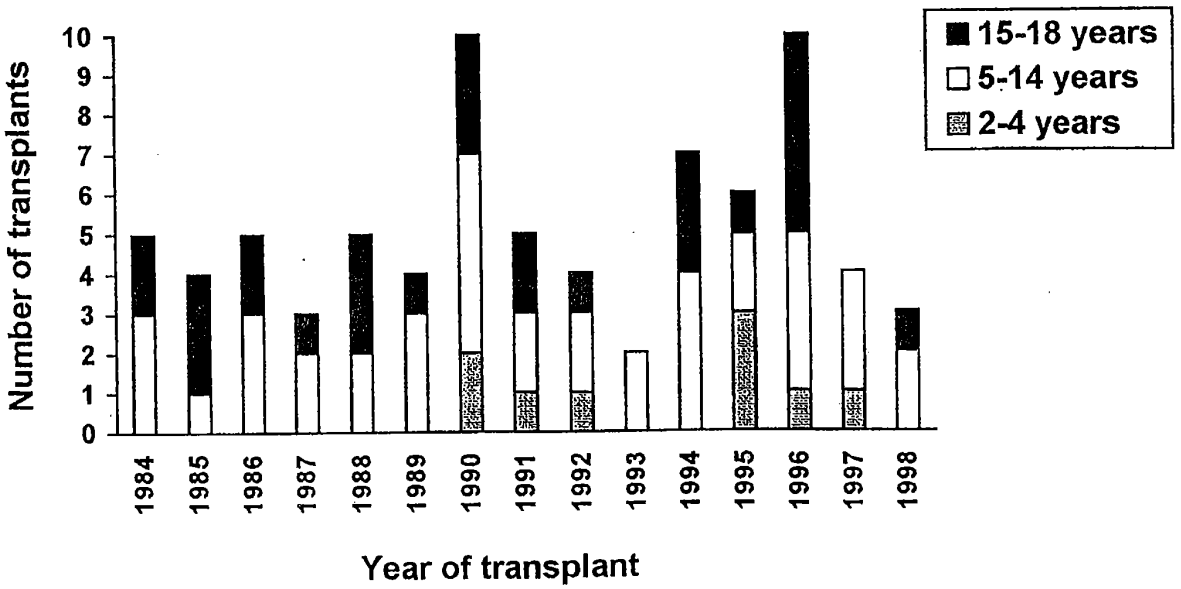

Fig 2. Paediatric cadaveric renal transplants in Belfast (1984-1998).

childhood with chronic pyelonephritis could be detected at an earlier phase by antenatal [3] and family screening [4,5] and early referral of children with proven urinary tract infections.[6,7] Table II lists the other commonest causes which are very similar to the range of conditions encountered nation-wide. The Northern Ireland figures are obviously much smaller, and the apparent predominance of chronic pyelonephritis is not significant.

TABLE II

Primary renal disease leading to transplantation in 77 patients in Northern Ireland (1983-1998), compared with percentage figures for UK/Republic of Ireland (1984-1993).

Primaryrenal disease	*Total*	*Percentage of total (77)*	*Percentage of total in UK/ Republic of Ireland (1406)*
Glomerulonephritis	7	9%	12%
Pyelonephritis, chronic	31	40.3%	28%
Polycystic kidneys, infantile	1	1.3%	2%
Medullary cystic disease	1	1.3%	3%
Hereditary nephropathy	8	10.4%	1%
Alports syndrome	1	1.3%	1%
Cystinosis	1	1.3%	3%
Congenital renal hypoplasia	2	2.6%	6%
Congenital renal dysplasia +/- urinary tract malfommation	3	3.9%	10%
Others	22	28.6%	34%

During the 15 year period the age range of the donors has been changing from a predominantly adult to a child population. This can be partly explained by the fact that in 1990 a new rule meant that a donated paediatric kidney was offered firstly to a paediatric patient. This change may also be partly explained by the increasing awareness of the medical profession and public alike of the need for organ donation, even when the potential donor is a dying child.

The age group of the recipient has also been changing during the 15 year period. Prior to 1990 all recipients were five years or older, but the 2-4 age group has seen an average of one transplant per year since then (figure 2). These nine transplants have become possible due to improving surgical techniques and because aggressive medical treatment of congenital nephrotic syndrome,[8] and end-stage renal failure in neonates has enabled survival to a size and weight compatible with transplantation. A major contribution to patient-survival is the introduction of intensive skilled nutritional support including the use of night-time tube feeding via gastrostomy, and peritoneal dialysis techniques in infants as small as 1000 grams. The Paediatric team while having reservations about the developmental outcome of babies treated for chronic renal impairment from infancy, has demonstrated the ability to dialyse and transplant these infants.

The median waiting times on the transplant list have gradually increased in each successive 5 year period, initially being about 3 months but by the late 1990's extending to about 11 months. This of course is not a problem unique to Northern Ireland. Despite national publicity campaigns organ demand continues to outstrip donation. Live donation is an alternative which has been underway for decades; locally a total of 5 such donations have taken place, 3 of which are still functioning.

Generally only a kidney with a haplotype tissue type match is considered and ideally a match on both DR loci is sought. Not every kidney offered therefore will be accepted, and on average 8 were turned down each year. Figure 3 shows that, as expected, the commonest reason by far is that a better match was required. Other factors to be considered include a prolonged ischaemic time (>24 hours) or adverse anatomical reasons e.g. in one case a tear in the renal vein meant that the operation would be technically difficult. It is unfortunate that 8 offers had to be declined because of lack of resources. In practice this usually meant the lack of a post-operative intensive-care bed or that key consultant nephrology or surgical staff were not available. This is a problem that is seen throughout the UK and Republic of Ireland where about 4% of offers are turned down for this reason.[2]

Of the 77 paediatric transplants in Belfast we have seen seven fail in the first 7 days post-

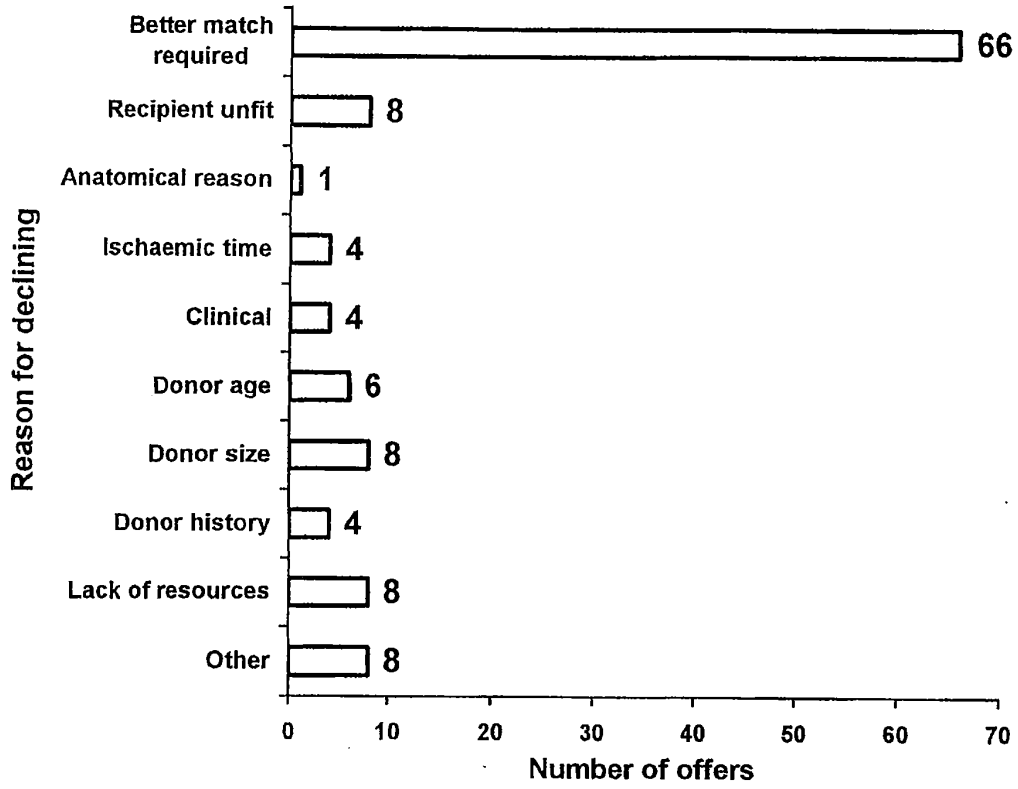

Fig 3. Reasons for declining paediatric kidney offers to Belfast (1984-1998).

transplant and an additional three in days 8 to 30, amounting to 13%. Guy's hospital for example has seen 45 fail in the first 30 days post transplant [2] accounting for 19% of the total (these statistics cover the period 1983-1994). The classifications of causes of graft failure shown in Table III are those employed by the UK Transplant Support Service. Initially a proportion of kidneys may be lost immediately following surgical placement due to an overwhelming immunological reaction. These are classified under the general title of hyperacute rejection. We believe this grouping fails to distinguish in our patients between severe immunological rejection, and early vascular thrombosis possibly caused by technical problems with the anastomosis. In 10% the primary cause of renal failure has recurred, usually glomerulonephritis. The apparent difference in the proportion of local patients suffering from rejection whilst on immunosuppression compared to nationwide figures, (Table III) is likely on review to result from a local anomaly in data reporting. The Belfast graft losses on immunosuppression are probably similar but hidden within the "other" category.

Two deaths, both occurring in the early postoperative period, represent a mortality rate of 2.6%. The causes of death were (a) fluid overload and (b) ARDS (Acute Respiratory Distress Syndrome.) In the UK and Republic of Ireland 48 deaths occurred in the 10 year period 1984-1993 giving a mortality rate of 3.4%, the 4 commonest causes of death being cardiac arrest (15%), fluid overload (13%), pulmonary infection (10%) and septicaemia (8%).[2] An ongoing audit of causes of early graft loss and death has led to refinement of transplant protocols in order to improve outcome.

Initially all children were immunosuppressed with prednisolone and azathioprine in combination until the mid 1980's. When cyclosporin became available it was an important milestone, which led to improved graft survival.[9] This drug works by inhibiting the transcription of interleukin 2 and thus early T cell activation. The use of cyclosporin became routine in our children despite initial dosage difficulties related to variable metabolism in childhood. Nephrotoxicity is avoided by careful blood level monitoring but

TABLE III

Cause of graft failure in Northern Ireland, (1984-1998), compared to graft failure in the UK/Republic of Ireland (1984-1993).

Cause of failure	*Northern Ireland*	*UK/ Republic of Ireland*
Hyperacute rejection	14%	2%
Rejection while on immunosuppressive drugs	29%	67%
Recurrent primary renal disease	10%	3%
Vascular or ureteric operative problems	5%	8%
Vascular thrombosis	19%	12%
Other	23%	8%

side-effects causing persistent and occasionally unacceptable problems are hirsutism and gum hypertrophy. More recently Tacrolimus, (a macrolide antibiotic) an agent with immunosuppressive activity approximately 100 times that of cyclosporin,[10] has become established as an efficacious drug in this field in which side-effects (e.g. nephrotoxicity and neurotoxicity) are reversible with dosage reduction.[11]

Of the children currently attending the RBHSC transplant follow-up clinic the mean standard deviation score for height is -0.83, with a range of -2.3 to +1.4. Only two children have a standard deviation score of less than -2, both of whom have been in chronic renal failure since infancy. This reflects careful attention to renal bone disease (using phosphate binders and vitamin D analogues), nutrition and the use of human growth hormone[12] in these children, and is one of the most dramatic improvements in this age group. Eradication of short stature as a result of chronic renal impairment and renal osteodystrophy is potentially achievable in all patients who can comply with modern treatment regimens.

CONCLUSION

Our figures demonstrate that in terms of short and long term graft survival and mortality Belfast is comparable to any similar centre nation-wide. Advances have been made during the 15 year period, most noticeably in the youngest children receiving transplantation. It is clear that a successful end stage renal replacement programme for children is achievable in a small geographical area with a limited population. There are advantages of an association with an adult unit, but the special needs of chronically ill children and demands for professional family support require the skills of a paediatric medical environment. Concerns for the future must focus on the ever-increasing waiting time and the shortage of donated organs, which are not problems restricted to Northern Ireland. Living related donation is part of the solution, and of course xenotransplantation may prove to be a controversial solution in the 21st century and is at present being evaluated.[13]

ACKNOWLEDGEMENT

The statistics in this paper were prepared by the UK transplant Support Service Authority from the National Transplant Database. The authors wish to acknowledge the role played by the adult nephrology service in providing help, advice and support that continue to benefit the paediatric dialysis and transplant programme. A particular debt of gratitude is owed to all the transplant surgeons, most recently Mr John Connolly.

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RENAL TRANSPLANT AUDIT

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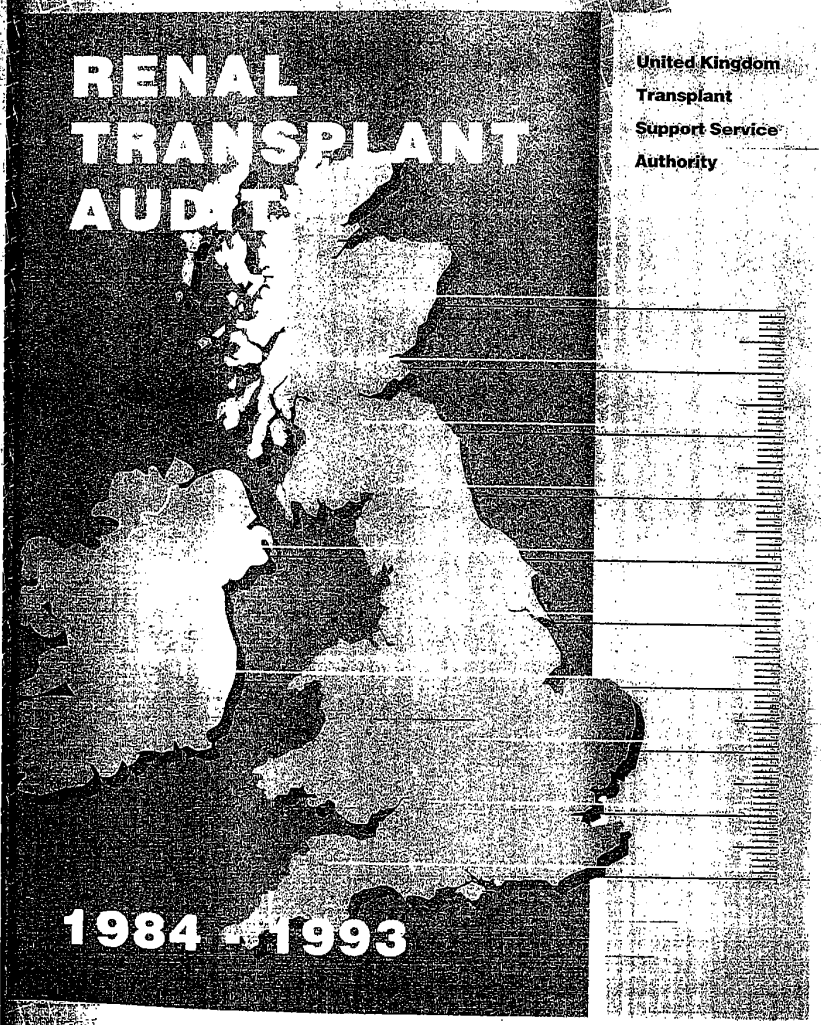

1984 - 1993

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Contents

Renal Transplant Audit 1984 - 1993

Appendices

An Overview

This Report represents a comprehensive Audit of renal transplantation in the UK and Republic of Ireland during the 10 years 1984 - 1993. At the time of publishing the first report in 1993, 14 centres had returned follow-up data on fewer than 25% of grafts: that number has reduced to 8 centres so that the completeness and validity of the data and analyses are much improved, but still far from ideal.

Comparison of the primary renal disease of patients grafted between 1984 and 1988 and during the following 5 years revealed that fewer patients with glomerulonephritis (GN) were grafted after 1989. For the same two intervals, the number not histologically examined fell from 50% to 30%. The incidence of GN in patients with end stage renal disease (ESRD) in the UK remains constant at around 15%, thus one explanation for the reduction observed could be the removal of a backlog of GN patients awaiting transplant. Recipients with diabetes, as a percentage of those grafted, remained constant at around 9%, although the incidence of diabetics with ESRD is increasing in the UK. An increase has been seen in the number of insulin dependent patients grafted since 1989 (81%) compared with the previous 5 years (53%). The mean age of non-insulin dependent recipients is also increasing (51 years for grafts since 1989, 43 years previously); this trend may reflect, at least in part, a change in referral pattern.

Analysis of causes of graft failure identified a significant reduction in graft rejection while taking immunosuppressive drugs, both acutely (in the first 3 months) and thereafter. However, increased numbers of graft failures due to vascular thrombosis were noted, with 92% of them occurring within 3 months. This effect may well reflect improved classification through the use of diagnostic ultrasound, rather than implicating any thrombotic effect of drugs or altered surgical techniques.

Multi organ donation increased substantially over the 10 years, from 22% of donors in 1985 to 68% in 1993. The number of donors dying from intracranial causes also increased steadily, while the number of trauma victims providing donor organs declined significantly since 1990 following the introduction of legislation governing the wearing of rear seat belts. These trends were coupled with a steady rise in the use of kidneys from older donors, although considerable variation in retrieval rates across centres remains.

Damage to the donor kidney continues to be an issue of concern and is closely monitored by the Kidney Advisory Group. Over the 4 years to 1993, damage was reported as the reason for the non-use of 11% of the small number of kidneys not transplanted. Significantly fewer damaged kidneys were retained locally compared with those exchanged, but no evidence was found to suggest that liver donation was associated with kidney damage or that the survival of reportedly damaged kidneys was

Overall, cadaveric donation levels have plateaued since 1990 at around 900 donors per annum, while waiting lists continue to rise. The gravity of the ever widening gap between supply and demand prompted the British Transplantation Society (BTS) to establish a working party to investigate the issues surrounding organ donation. While several initiatives aimed at improving the situation were highlighted, the supply of cadaveric human organs is unlikely to meet the demand given current selection criteria and referral policies for transplantation. Much variation exists between centres in terms of waiting list size, relative both to the population served and to the percentage of dialysis patients awaiting transplantation. The Report shows that median waiting time for adults has increased each year since 1989: referral for transplantation may be unrealistic for some patients.

Analysis of offers of kidneys to centres over the four years to 1993 revealed, not unexpectedly, that the number of offers received was related both to waiting list size and to balance of exchange status. Some exceptionally large balances had accrued, indicating that for these centres their use of kidneys differed markedly from their retrieval ability. Although the proportion of beneficially matched kidneys not used for the intended recipient was very small (4%), indicating that centres are generally committed to the benefit of HLA matching, the variability between centre balances brings into question both the long term viability of some and equitability of the exchange scheme. Indeed, a Task Force of the Kidney Advisory Group has been established to review future parameters and priorities for kidney sharing in the UK.

'Recipient unfit' was a common reason given for a centre declining an offered kidney, suggesting that full use is not being made of the 'suspended' category. Since temporarily suspended patients are excluded from consideration, its routine use prevents time being lost while the kidney is offered inappropriately and also helps to minimise ischaemia times. A positive cross-match remained the main reason for the non-use of accepted kidneys. Improved screening and greater use of the 'unacceptable antigen' declaration could help to minimise this and thereby to reduce the incidence of inappropriate kidney sharing in the future.

Analyses of factors associated with transplant survival constitute a major part of the Audit. While success rates have improved significantly over time, [illegible] and the use of right donor

RENAL TRANSPLANT AUDIT 1984 - 1993

An Overview

kidneys together with those from older (>55 years), younger (<19 years), non-trauma and CMV positive donors continue to carry significantly increased risks of failure. Female donor to male recipient, exchanged and non-beneficially matched transplants, along with grafts given to younger and older recipients, are also associated with inferior overall survival. Analysis of distinct post transplant intervals further confirmed that for some factors the risk persists while others are transient.

Detailed analysis of the influence of HLA matching established that mis-matched transplants, and particularly those with 2 mis-matches at the A, B or DR locus, carry the risk of significantly inferior transplant survival, with the risk being greatest for DR mis-matched grafts. All matching effects were found to be transient; the persistent B locus effect previously identified from the Eurotransplant database was not confirmed. DR and B mis-matches were significant in the first 3 months and up to a year post transplant, respectively, while A mis-matches had greatest influence for grafts surviving beyond 1 year. A long term DR effect for grafts functioning 3+ years was also indicated. These findings differ from those presented previously, when the effect of A locus mis-matches was neither strong nor clear and a model involving the 9 B-DR combinations was found to be appropriate. The reason for this may be threefold: first, this analysis concentrated on transplant, rather than graft, survival as the outcome: secondly, this analysis included both longer term follow-up and 350 additional cases, and thirdly, the previous study included grafts in 1983 but not those in the latter 6 months of 1993.

While both older donors and recipients (>55 years) were identified as significant risk factors, the effect was not purely additive. The results suggested that kidneys from donors over 60 years fare better in recipients over 60 years than in recipients aged 46 - 60 years at transplant. Why this should be so is not entirely clear, but could be associated with reduced immune response and increased tolerance which occurs with age. Whatever the reason, at a time when kidneys are increasingly being retrieved from older donors, the optimum allocation of these kidneys is a matter for consideration.

Comparison of transplant survival estimates for each centre cohort revealed that 1 year survival estimates for grafts in the years 1984 - 1988 ranged from 68% to 86%, with a national average of 78%, while for grafts in the following 5 years the range was 72% to 89%, with national estimate 84%. Despite an overall improvement in survival, the variation across centres was broadly unchanged at one year. All available cases were used to calculate these estimates, but further study into the reasons for the differences found is warranted, including data on patients with no follow-up.

Delayed graft function (DGF) is a continuing problem in 28% of adult and 25% of paediatric grafts. The identified risk factors for the occurrence of DGF were similar to those for transplant survival, namely increasing donor age, right kidneys, those from male and non-trauma donors, exchanged and non-beneficially matched grafts, regrafts and male recipients. However, after adjusting for these known risks the survival of grafts with DGF was significantly inferior, indicating that other unidentified risk factors also exist.

Analysis of 1400 paediatric (<19 years) transplants reported established that, despite the current scheme which preferentially allocates paediatric organs to paediatric recipients, over 50% of 15 - 18 year olds received adult organs. Overall, paediatric waiting lists remain small at around 150 cases. The most common diagnoses leading to transplantation were pylonephritis/ interstitial nephritis (28%) and congenital renal dysplasia (10%). Transplant survival analysis revealed significant risk factors consistent with those identified from the full cohort. Kidneys from donors under 11 years were found to be particularly inferior, which brings into question the current allocation priorities. However, grafts in very young recipients (<6 years) surviving at least 3 months afforded superior survival compared with those in patients aged 6 - 18 years. The majority of graft failures were due to rejection; 40% of reported failures occurred within 30 days, with the number failing within 7 days increasing with decreasing age.

Living donor transplants continue to represent the most successful grafts. 96% of the two haplotype matched transplants reported over the 5 years since 1989 survived 1 year, and 93% were functioning at 3 years; 83% of those with no haplotype matches were functioning at 1 year and 72% survived beyond 3 years. The success of what is currently a very limited living donor programme is particularly notable. In view of the shortage of cadaveric kidneys, the programme deserves to be considered more seriously for a larger number of recipients.

UKTSSA
United Kingdom Transplant Support Service Authority

Professor P.J.Morris FRS
Chairman
UKTSSA Users' Kidney Advisory Group
June 1995

Table 13.3

Multifactorial analysis of kidney transplants for 788 donors over 60 years in the UK and Republic of Ireland, 1 January 1984 - 31 December 1993

Three year transplant survival - Epoch analysis

Factor	Level (Baseline)	0-41 days post transplant: Relative Risk	95% Confidence Interval	Prob	42-300 days post transplant: Relative Risk	95% Confidence Interval	Prob	300+ days post transplant: Relative Risk	95% Confidence Interval	Prob
Graft Number	(First)	1.00			1.00			1.0		
	Second	1.64*	1.00-2.68	0.05	0.74	0.31-1.80	0.51	1.43	0.77-2.68	0.26
	Third+	1.70	0.40-7.26	0.47	1.63	0.20-12.96	0.64	1.00		0.99
Year of Transplant	(1984-1986)	1.00			1.00			1.00		
	1987-1989	0.56*	0.34-0.93	0.03	1.25	0.58-2.69	0.56	1.49	0.84-2.64	0.17
	1990-1993	0.41*	0.25-0.66	0.03	0.87	0.41-1.84	0.71	1.07	0.55-2.10	0.83
Recipient Age at Transplant (years)	19-45	0.77	0.45-1.31	0.33	0.32*	0.16-0.66	0.002	1.47	0.75-2.88	0.26
	46-60	0.93	0.57-1.75	0.78	0.76	0.43-1.32	0.32	1.64	0.86-3.12	0.13
	(>60)	1.00			1.00			1.00		
Sex Match	Other Female Donor to Male Recipient	1.00			1.00			1.00		
		0.99	0.67-1.45	0.95	1.54	0.97-2.46	0.07	1.42	0.89-2.25	0.14
Donor Cause of Death	(Trauma)	1.00			1.00			1.00		
	Non-trauma	1.03	0.65-1.64	0.88	1.28	0.61-2.66	0.51	0.84	0.49-1.46	0.54
Donor Kidney	(Left)	1.00			1.00			1.00		
	Right	0.96	0.67-1.38	0.83	0.88	0.54-1.42	0.60	0.89	0.57-1.38	0.60
Matching	(Beneficial)	1.00			1.00			1.00		
	Non-beneficial	1.91*	1.14-3.18	0.01	1.60	0.81-3.15	0.18	2.05*	1.13-3.70	0.02
Shipping	(Local)	1.00			1.00			1.00		
	Imported	1.69*	1.14-2.50	0.009	1.08	0.64-1.82	0.78	0.99	0.61-1.61	0.96

* Significant from baseline

14.1 Introduction

14.2 Paediatric Transplant Activity

Table 14.1

Cadaveric kidney transplants in recipients aged 0-18 years at the time of transplant in the UK and Republic of Ireland reported to UKTSSA, 1 January 1984 - 31 December 1993, by centre

Recipient Centre	Year of Transplant 1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	TOTAL
Newcastle	5	7	10	4	8	5	4	7	6	9	65
Leeds	10	13	6	7	13	8	7	10	7	16	97
Leicester	1	1	6	2	-	2	1	2	1	1	17
Nottingham	3	4	7	3	4	2	5	4	8	10	50
Sheffield	5	6	1	2	1	1	4	1	2	2	25
Cambridge	4	3	3	2	7	1	2	2	1	3	28
St Mary's	2	-	-	-	1	1	2	-	1	1	8
Charing Cross	-	-	-	-	-	-	-	1	-	-	1
Hammersmith	1	-	-	2	-	-	-	-	-	-	3
The Royal Free	3	11	11	18	15	14	17	14	14	14	131
St Peter's	-	-	-	-	-	-	2	-	-	-	2
St Bartholomew's	1	2	-	1	1	-	-	-	-	-	5
Royal London	1	1	1	-	2	-	-	-	-	-	5
Great Ormond St	-	-	-	-	-	7	5	10	5	4	31
Brighton	-	-	-	-	-	-	-	1	2	-	3
St Thomas'	1	-	-	-	-	-	-	-	-	-	1
Dulwich	2	2	1	1	-	-	3	1	1	-	11
Guy's	47	29	29	27	20	23	10	22	13	18	238
St Helier	-	-	-	1	1	-	-	-	-	-	2
Portsmouth	-	3	4	5	1	2	-	-	1	1	17
Oxford	1	1	-	-	2	2	-	1	1	1	9
Bristol	3	7	13	5	3	6	1	5	6	7	56
Exeter	-	-	1	1	-	-	-	-	1	-	3
Plymouth	-	-	1	-	-	1	-	-	2	1	5
Stoke	1	-	-	-	-	-	-	1	1	-	3
Birmingham	13	16	9	9	12	10	6	6	18	18	117
Coventry	-	-	-	-	1	1	-	2	1	-	5
Liverpool	3	5	2	5	2	5	1	-	2	1	26
Manchester	15	8	18	8	20	17	6	11	7	22	132
Cardiff	6	4	4	3	8	11	7	4	4	7	58
Glasgow	11	5	9	9	11	6	8	7	6	7	79
Aberdeen	3	4	1	5	-	4	3	2	1	1	24
Edinburgh	1	2	1	2	3	3	1	1	1	2	17
Dundee	-	-	-	-	-	1	-	-	-	1	2
Belfast	5	4	5	3	5	4	10	5	4	2	47
Dublin	5	5	4	3	7	12	12	16	11	8	83
TOTAL	153	143	147	128	148	149	117	136	128	157	1406

Figure 14.1

Cadaveric kidney transplants in paediatric recipients in the UK and Republic of Ireland reported to UKTSSA, 1 January 1984 - 31 December 1993, by centre

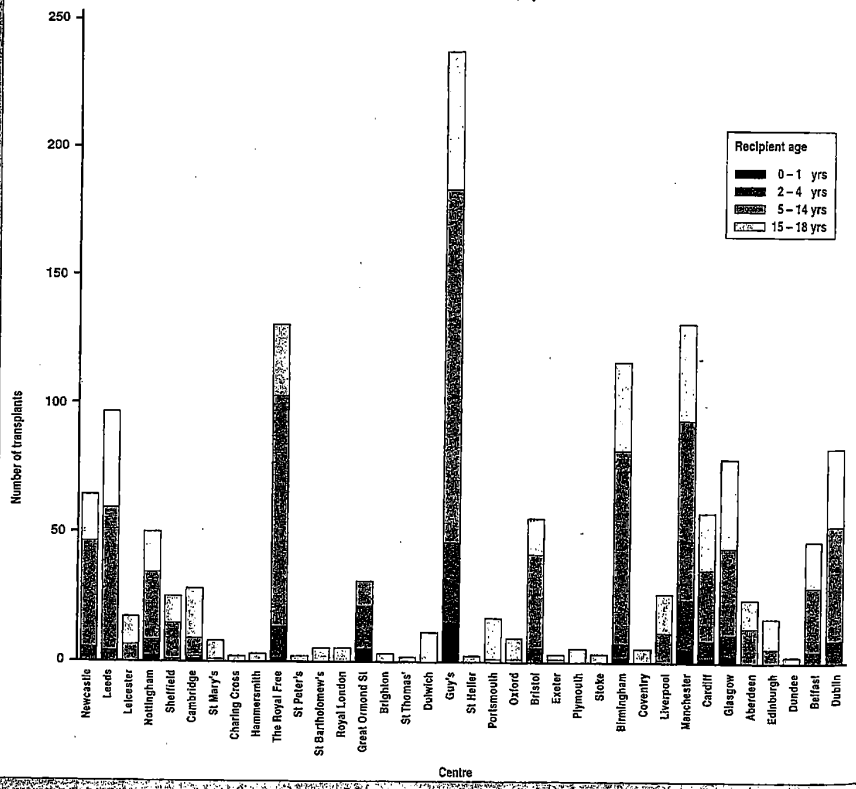


Figure 14.2

Cadaveric kidney transplants in paediatric recipients in the UK and Republic of Ireland reported to UKTSSA, 1 January 1984 - 31 December 1993, by year of transplant

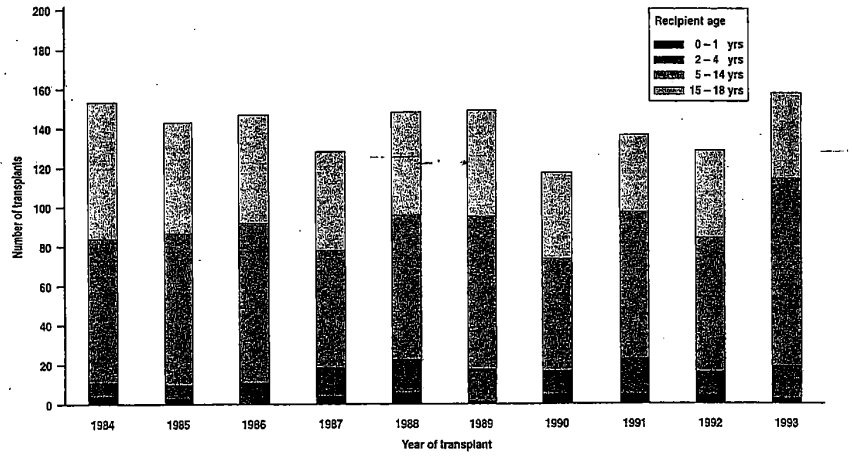
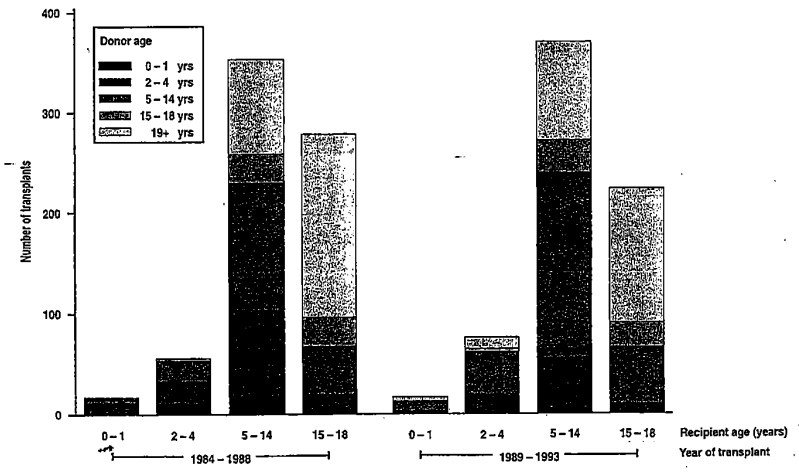


Figure 14.3

Cadaveric kidney transplants in paediatric recipients in the UK and Republic of Ireland reported to UKTSSA, 1 January 1984 - 31 December 1993, by donor age



14.3 Recipient Primary Renal Disease

The primary renal disease reported for recipients of cadaveric kidney transplants reported between 1984 and 1993 is shown in **Table 14.2**. Primary disease was available for 1023 grafts (79% of all grafts reported). Those diseases with a frequency of less than 10 have been grouped into 'other identified renal disorders'. The most common primary disease reported were dysplasia/hypoplasia/aplasia (28% of cases, 29%) and congenital renal dysplasia with or without urinary tract malformation (10%).

14.4 Causes of Transplant Failure and Patient Death

Of the 1406 paediatric cadaveric transplants reported between 1984 and 1993, 439 (31%) were reported as failed at the time of audit (excluding deaths with a functioning graft). A cause of failure was reported for 373 (85%) of these failed grafts, as shown in **Table 14.3**. The majority of failures (72%) were due to rejection. However, failures due to rejection appear to be declining as the number of reported failures due to

Table 14.2

Primary renal disease for all paediatric cadaveric kidney recipients in the UK and Republic of Ireland reported to UKTSSA, 1 January 1984 - 31 December 1993, by year of transplant

Primary Renal Disease	Year of Transplant 1984-1988 No	%	1989-1993 No	%	TOTAL No	%
Glomerulonephritis, histologically not examined	37	6	5	1	42	4
Severe nephrotic syndrome with focal sclerosis	18	3	29	7	47	5
Glomerulonephritis, histologically examined	54	9	28	6	82	8
Pyelonephritis/interstitial nephritis - all cases	156	27	127	29	283	28
Polycystic kidneys, infantile (recessive)	10	2	10	2	20	2
Medullary cystic disease, including nephronophthisis	19	3	12	3	31	3
Hereditary/familial nephropathy - type unspecified	4	1	7	2	11	1
Hereditary nephritis with nerve deafness	10	2	4	1	14	1
Cystinosis	23	4	12	3	35	3
Congenital renal hypoplasia - type unspecified	43	7	23	5	66	6
Congenital renal dysplasia +/- urinary tract malformation	56	10	48	11	104	10
Syndrome of agenesis of abdominal muscle	10	2	3	1	13	1
Renal vascular disease - all type	8	1	4	1	12	1
Henoch-Schonlein purpura	14	2	6	1	20	2
Haemolytic uraemic syndrome	10	2	18	4	28	3
Other identified renal disorders	106	18	109	24	215	21
TOTAL	578	100	445	100	1023	100

14 Paediatric Analyses

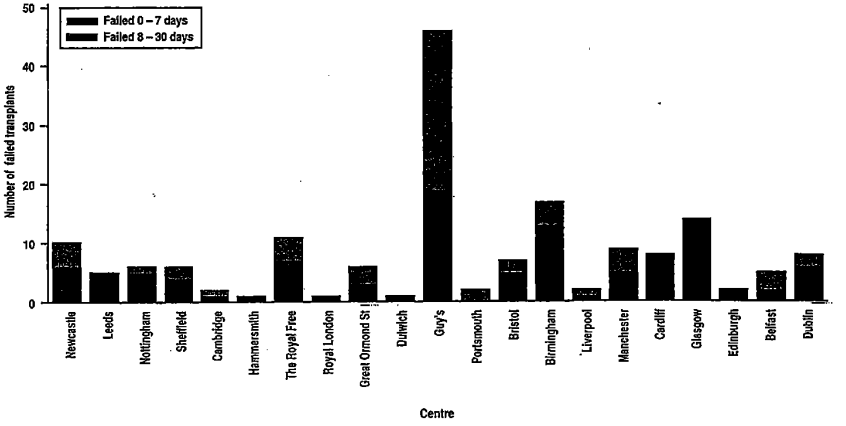
Table 14.3

Cause of graft failure for failed cadaveric kidney transplants in paediatrics in the UK and Republic of Ireland reported to UKTSSA, 1 January 1984 - 31 December 1993

Cause of Failure	Year of Transplant 1984-1988 No	%	1989-1993 No	%	TOTAL No	%
Hyperacute rejection	4	2	2	2	6	2
Rejection while taking immunosuppressive drug(s)	184	71	67	58	251	67
Rejection after stopping all immunosuppressive drug(s)	9	3	2	2	11	3
Recurrent primary renal disease	7	3	5	4	12	3
Vascular or ureteric operative problems	22	9	9	8	31	8
Vascular (arterial or venous) thrombosis	20	8	23	20	43	12
Infection of graft	3	1	-	-	3	1
Removal of functioning graft	1	0	2	2	3	1
'Non-viable' kidney	3	1	-	-	3	1
Other	5	2	5	4	10	3
TOTAL	258	100	115	100	373	100

Figure 14.4

Cadaveric kidney transplants failing in the first 30 days in paediatric recipients in the UK and Republic of Ireland reported to UKTSSA, 1 January 1990 - 31 December 1993, by centre



14 Paediatric Analyses

Figure 14.5

Cadaveric kidney transplants failing in the first 30 days in paediatric recipients in the UK and Republic of Ireland reported to UKTSSA, 1 January 1984 - 31 December 1993, by recipient and donor age

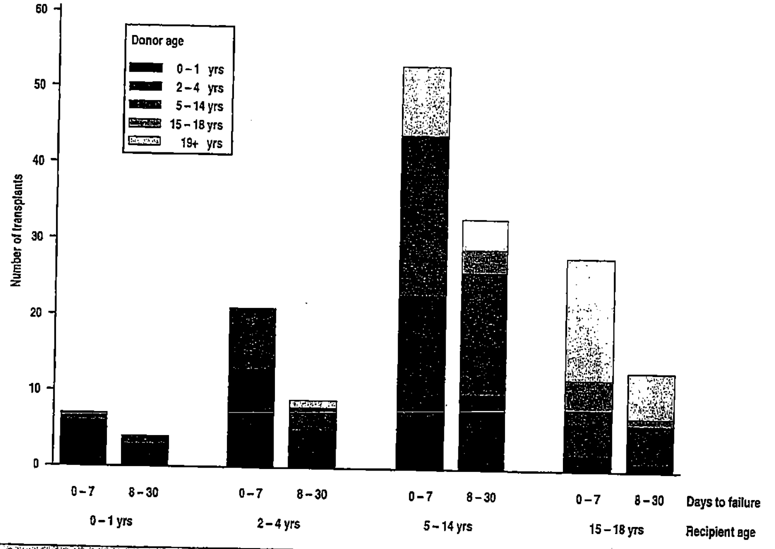


Table 14.4

Cause of death of paediatric cadaveric kidney transplant recipients in the UK and Republic of Ireland reported to UKTSSA, 1 January 1984 - 31 December 1993

Cause of Death	1984-1988 No	1984-1988 %	1989-1993 No	1989-1993 %	TOTAL No	TOTAL %
Myocardial ischaemia and infarction	3	9	-	-	3	6
Hyperkalaemia	3	9	-	-	3	6
Cardiac arrest, cause unknown	5	15	2	14	7	15
Hypokalaemia	-	-	1	7	1	2
Fluid overload	5	15	1	7	6	13
Other causes of cardiac failure	2	6	1	7	3	6
Cerebro-vascular accident	2	6	2	14	4	8
Haemorrhage from graft site	-	-	1	7	1	2
Pulmonary infection	3	9	2	14	5	10
Infections elsewhere (except viral hepatitis)	2	6	-	-	2	4
Septicaemia	2	6	2	14	4	8
Other identified cause of death	7	21	2	14	9	19
TOTAL	34	100	14	100	48	100

(Year of Transplant)

14 Paediatric Analyses

Of the 1202 paediatric patients receiving a cadaveric transplant in the ten years 1984-1993, 79 (7%) were reported to have died by the time of Audit. A cause of death was recorded for 48 (61%) of these deaths and these are documented in Table 14.4. Cardiac arrest (cause unknown) was the most frequently specified cause of death (15%).

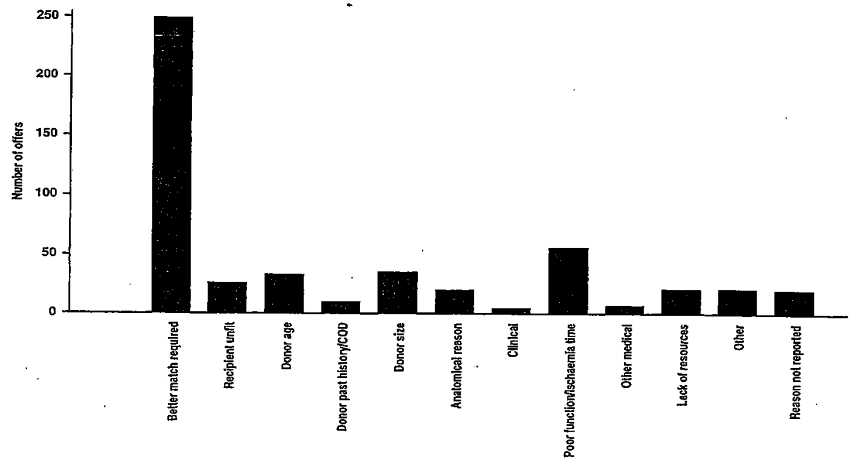
14.5 Offers of Kidneys for Paediatric Recipients

Over the four years 1990 - 1993, 890 kidney offers for paediatric recipients in the UK and Republic of Ireland were recorded by the UKTSSA Duty Office. Of these 890 offers, 29% were accepted and used, 14% were accepted for transplant but not subsequently used and 57% were declined. Centres receiving the greatest number of offers were Newcastle (11% of all offers), Leeds (11%), Guy's (9%) and Belfast (8%). Some centres received very few, if any, kidney offers for paediatric kidney recipients.

The reasons given for the 504 kidney offers declined are shown in Figure 14.6. The majority of offers (25[illegible], 49%) were declined because a better match was required while a further 56 (11%) were declined due to poor function or the ischaemia time.

Figure 14.6

Reasons for declining paediatric kidney offers to centres in the UK and Republic of Ireland reported to UKTSSA, 1 January 1990 - 31 December 1993

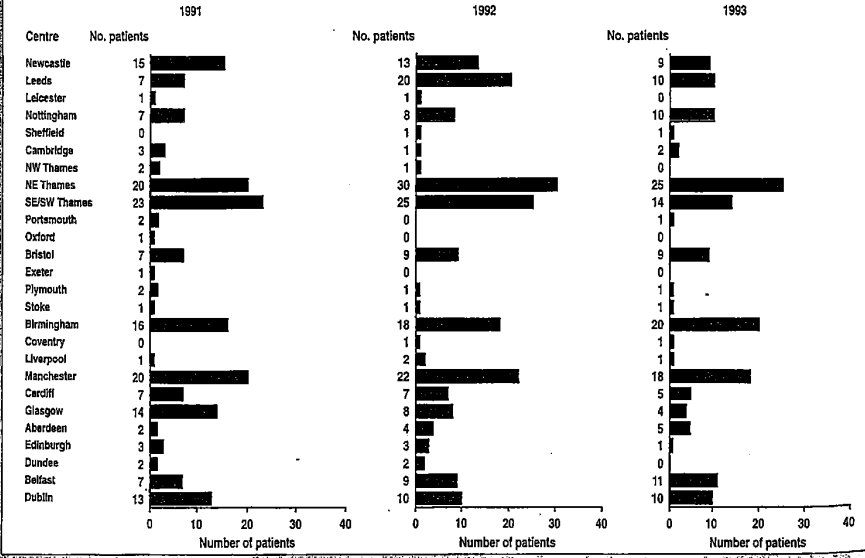


7.6 Waiting List at 31 December 1991, 1992 and 1993

Figure 14.7 shows the number of patients registered on the national active or suspended kidney transplant waiting list at 31 December 1991, 1992 and 1993, by centre. Figure 7.8 gives median waiting times to transplantation for paediatrics by centre and Figure 7.9 compares the median waiting time for adult and paediatric recipients for patients registered during each year of the 10 study period.

Figure 14.7

Number of paediatric patients in the UK and Republic of Ireland on the active or suspended national kidney transplant waiting list, at 31 December 1991, 1992 and 1993, by centre



7.7 National Outcome Analyses

Table 14.5

Multifactorial analysis of cadaveric kidney transplants in paediatrics in the UK and Republic of Ireland, 1 January 1984 - 31 December 1993

Overall Transplant Survival

Factor	Level Baseline	Relative Risk	95% Confidence Interval	Prob
Graft Number	(First)	1.00		
	Regraft	1.13	0.90-1.43	0.30
Year of Transplant	(1984-1986)	1.00		
	1987-1989	0.97	0.78-1.22	0.8
	1990-1993	0.65*	0.49-0.86	0.003
Recipient Age at Transplant (years)	(15-18)	1.00		
	0-4	1.06	0.74-1.52	0.8
	5-14	0.81	0.64-1.03	0.09
Donor Age (years)	(19+)	1.00		
	0-1	3.04*	1.91-4.84	0.0001
	2-4	1.55*	1.12-2.14	0.009
	5-10	1.42*	1.04-1.9	0.03
	11-14	1.03	0.70-1.51	0.9
	15-18	0.82	0.54-1.24	0.3
Donor Cause of Death	(Trauma)	1.00		
	Non-trauma	1.25*	1.02-1.54	0.03
Matching	(Beneficial)	1.00		
	Non-beneficial	1.92*	1.32-2.81	0.0007
Shipping	(Local)	1.00		
	Imported	1.04	0.84-1.29	0.7

... three recipient age groups shown in Table 14.5. For the study of donor age the 5 - 14 years age group was further subdivided into donors aged 5 - 10 years and those aged 11 - 14 years. Differences between these two groups were found as shown in Table 14.5.

An epoch analysis focusing on the two post transplant intervals (0 - 3 months and 3+ months) was also carried out to assess possible changes in risk over time. For overall transplant survival somewhat surprisingly recipient age was not identified as a significant risk factor. The epoch analysis served to highlight why this was so: in the first 3 months post transplant recipients under 5 years of age were found to carry a much increased risk of transplant failure (compared with the baseline group of 15 - 18 year olds), but for those grafts surviving beyond 3 months the risk of failure for these very young recipients was significantly reduced, as was the risk for those aged between 5 and 14 years (see **Figure 14.8**). This change in risk served to mask the effect in the overall survival model. Kidneys from donors under 10 years of age carry a much increased risk for overall survival and in the early post transplant period, while the effect of donor cause of death is greatest for transplants surviving beyond 3 months.

Figure 14.8

Multifactorial analysis of cadaveric kidney transplants in paediatrics in the UK and Republic of Ireland, 1 January 1984 - 31 December 1993

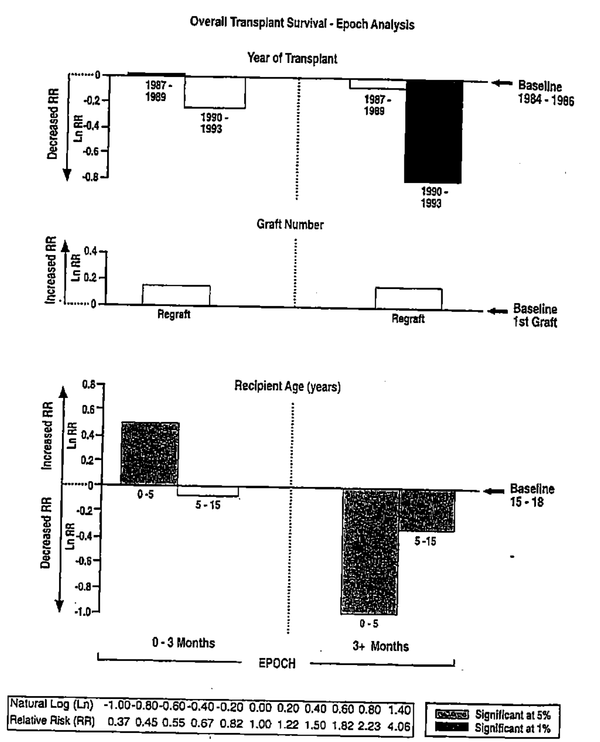


Figure 14.8 continued

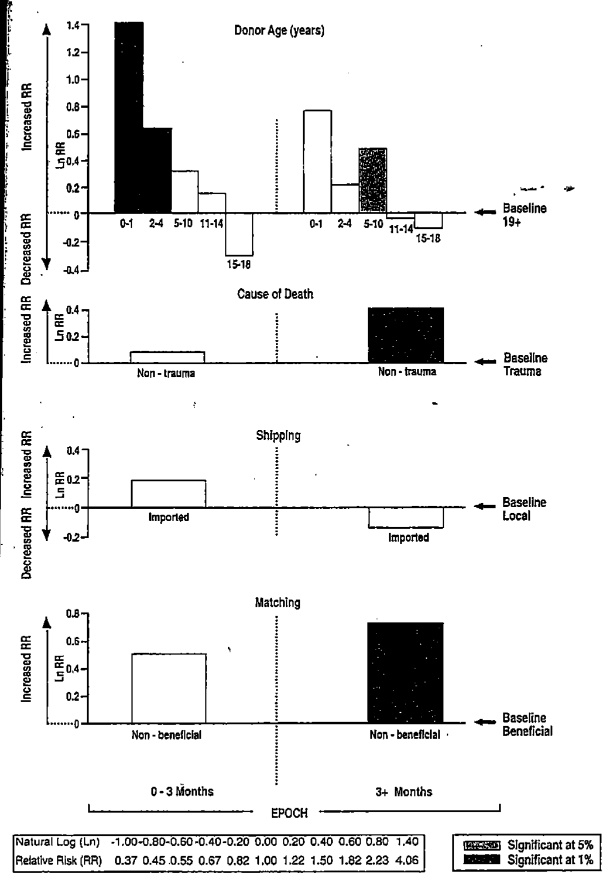


Table 14.6

One and five year transplant survival after cadaveric kidney transplant in paediatrics in the UK and Republic of Ireland, 1 January 1984 - 31 December 1993

Graft Number	Number at Risk at Day 0	One Year % Survival	One Year 95% Confidence Interval	Five Years % Survival	Five Years 95% Confidence Interval
First	914	75	72-78	61	57-64
Regraft	250	73	68-79	60	54-67

Table 14.7

One and five year transplant survival after first cadaveric kidney transplant in paediatrics in the UK and Republic of Ireland, 1 January 1984 - 31 December 1993

Factor	Level	Number at Risk at Day 0	One Year % Survival	One Year 95% Confidence Interval	Five Years % Survival	Five Years 95% Confidence Interval
Year of Transplant	1984-1986	306	73	68-78	58	52-63
	1987-1989	289	72	67-77	57	51-63
	1990-1993	319	80	76-85		
Recipient Age at Transplant (years)	0-4	119	60	51-68	55	45-65
	5-14	489	76	72-80	61	56-66
	15-18	306	80	75-84	62	56-69
Donor Age (years)	0-1	33	36	20-53	25	10-41
	2-4	152	58	50-66	48	39-56
	5-10	226	74	69-80	62	54-69
	11-14	99	82	74-90	65	53-77
	15-18	83	89	82-96	68	55-80
	19+	321	82	78-86	67	61-73
Donor Cause of Death	Trauma	510	77	73-81	65	60-69
	Non-trauma	404	73	68-77	55	49-61
Matching	Beneficial	112	88	82-94	76	65-87
	Non-beneficial	802	73	70-76	58	54-62
Shipping	Local	438	79	75-83	62	57-67
	Imported	476	72	68-76	59	54-65

14 Paediatric Analyses

Figure 14.9

Five year transplant survival after cadaveric paediatric kidney transplant in the UK and Republic of Ireland, 1 January 1984 - 31 December 1993, by graft number

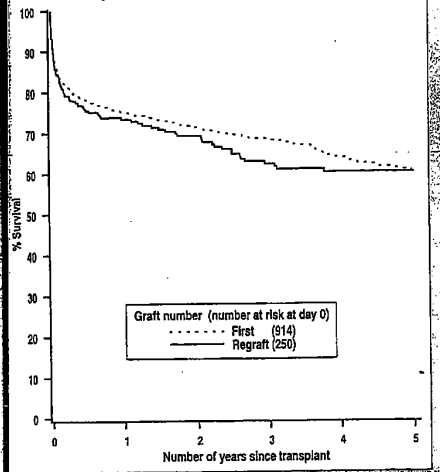


Figure 14.10

Five year transplant survival after first cadaveric paediatric kidney transplant in the UK and Republic of Ireland, 1 January 1984 - 31 December 1993, by year of transplant

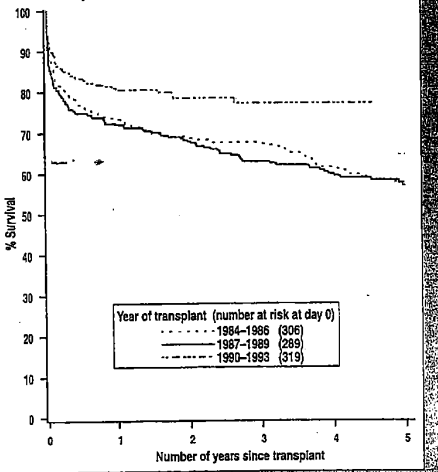


Figure 14.11

Five year transplant survival after first cadaveric paediatric kidney transplant in the UK and Republic of Ireland, 1 January 1984 - 31 December 1993, by recipient age at transplant

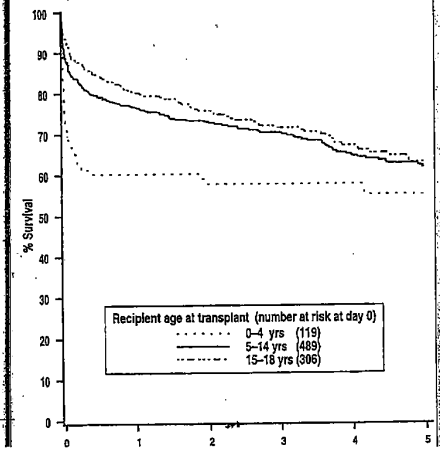
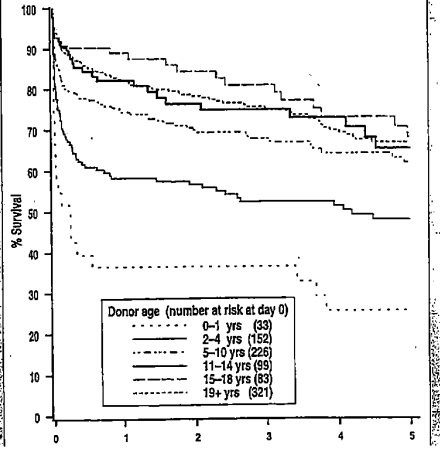


Figure 14.12

Five year transplant survival after first cadaveric paediatric kidney transplant in the UK and Republic of Ireland, 1 January 1984 - 31 December 1993, by donor age



14 Paediatric Analyses

Figure 14.13

Five year transplant survival after first cadaveric paediatric kidney transplant in the UK and Republic of Ireland, 1 January 1984 - 31 December 1993, by donor cause of death

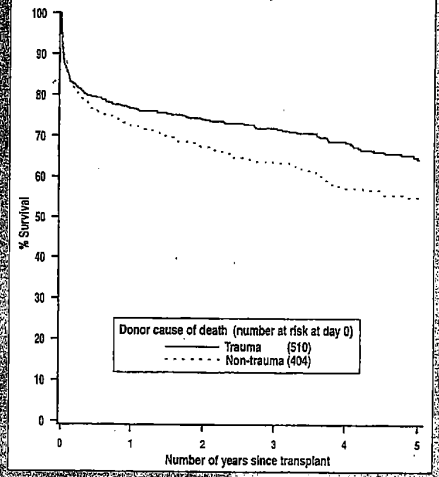


Figure 14.14

Five year transplant survival after first cadaveric paediatric kidney transplant in the UK and Republic of Ireland, 1 January 1984 - 31 December 1993, by HLA matching

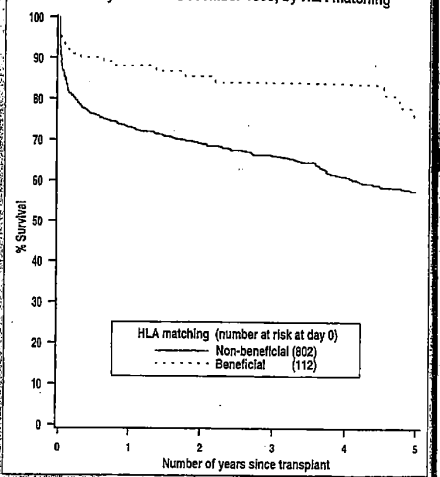
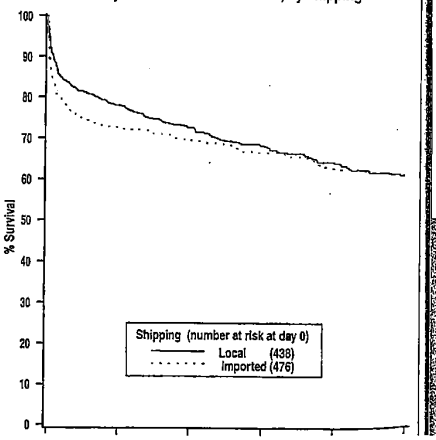


Figure 14.15

Five year transplant survival after first cadaveric paediatric kidney transplant in the UK and Republic of Ireland, 1 January 1984 - 31 December 1993, by shipping



15 Long Term Transplant Survival

Table 15.1

Ten year transplant survival after cadaveric kidney transplant in the UK and Republic of Ireland, 1 January 1981 - 31 December 1993

Graft Number	% Survival	95% Confidence Interval	Number at Risk at Day 0
First	45	44-47	13191
Second	43	39-46	2294
Third +	34	25-43	421

Table 15.2

Ten year transplant survival after first cadaveric kidney transplant in the UK and Republic of Ireland, 1 January 1981 - 31 December 1993

Factor	Level	% Survival	95% Confidence Interval	Number at Risk at Day 0
Year of Transplant	1981-1983	39	37-41	2272
	1984-1986	42	39-44	3065
	1987-1989	-	-	-
	1990-1993	-	-	-
Recipient Age at Transplant (years)*	<19	44	39-48	1206
	19-55	48	46-49	9377
	56+	33	28-38	2587
Sex Match	Female Donor to Male Recipient	39	36-42	3333
	Other	47	45-49	9858
Donor Age (years)+	<19	46	43-49	2902
	19-55	47	45-49	8672
	56+	35	30-40	1557
Donor Cause of Death	Trauma	47	44-49	5644
	Non-trauma	44	42-46	7547
Donor Kidney	Left	46	44-49	6687
	Right	44	42-46	6504
Matching	Beneficial	53	48-58	2201
	Non-beneficial	44	42-45	10990
Shipping	Local	46	44-47	8410
	Imported	44	42-47	4781

* 21 missing
\+ 60 missing

[illegible] transplant survival estimates for transplants grouped according to the donor and recipient factors evaluated are given in **Tables 15.1** and **15.2**. Kaplan-Meier plots illustrating transplant survival to 13 years post transplant are given in **Figures 15.1** to **15.10**. These survival plots demonstrate the possible long term effects of each single factor on survival after first cadaveric transplant, excepting **Figure 15.1** which shows overall survival for first and regrafts. The plots show trends consistent with those illustrated in Section 10 for five year transplant survival, and do not suggest any changing effects of note beyond that time.

(a) Identify precisely on Adam's medical notes and records the entries in your handwriting.

DATE	REF NO	NOTE	SIGNED
15-10-91	(049-029-076)	OUTPATIENT	MAURICE SAVAGE
16-10-91	(049-029-079)	ASTRUP REQUEST	UNSIGNED
08-11-91	(049-029-088)	8.30pm	M SAVAGE
26-11-91	(049-029-081)	FAMILY HISTORY	UNSIGNED
28-11-91	(049-029-087)	CLINICAL NOTE RE DIALYSIS	M SAVAGE
29-11-91	(049-029-089)	CLINICAL	M SAVAGE
30-11-91	(049-029-090)	CLINICAL	MS
01-12-91	(049-029-091)	CLINICAL	M SAVAGE
03-12-91	(049-029-092)	PLAN TODAY	MS
12-12-91	(049-029-100)	CLINICAL	M SAVAGE
15-12-91	(049-029-102)	CLINICAL	MS
17-12-91	(049-029-105)	CLINICAL	MS
19-12-91	(049-029-106)	HYPERNATRAEMIC	UNSIGNED
27-11-91 to 27-02-92	(050-018-051 to 055)	INVESTIGATION SUMMARY SHEETS	UNSIGNED
22-12-91	(050-023-067)	CLINICAL	SIGNATURE OBSCURED
23-12-91	(050-023-070)	CLINICAL	MS
24-12-91	(050-023-071)	CLINICAL	MS
27-12-91	(050-023-072)	CLINICAL	MS
30-12-91	(050-023-074)	CLINICAL	MS

31-12-91	(050-023-074)	CLINICAL	MS
Jan 92-Feb 92	(050-016-048)	INVESTIGATION SUMMARY SHEETS	UNSIGNED
06-01-92	(050-023-076)	CLINICAL	MS
07-01-92	(050-023-077)	CLINICAL	M SAVAGE
09-01-92	(050-023-077)	CLINICAL	MS
10-01-92	(050-023-078)	CLINICAL	UNSIGNED
13-01-92	(050-023-080)	CLINICAL	MS
22-01-92	(050-023-083)	CLINICAL	MS
23-01-92	(050-023-083)	CLINICAL	MS
27-01-92	(050-023-084)	CLINICAL	MS
30-01-92	(050-023-085)	CLINICAL	MS
03-02-92	(050-023-085)	CLINICAL	MS
04-02-92	(050-023-085)	CLINICAL	MS
07-02-92	(050-023-087)	CLINICAL	MS
08-02-92	(050-023-087)	CLINICAL	MS
12-02-92	(050-023-091)	CLINICAL	M SAVAGE
14-02-92	(050-023-092)	CLINICAL	M SAVAGE
18-02-92	(050-023-093)	CLINICAL	MS
24-02-92 & 25-02-92)	(052-023-044)	CLINICAL	MS
02-03-92	(052-023-046)	CLINICAL	UNSIGNED
06-03-92	(052-023-047)	CLINICAL	MS
16-03-92 & 17-03-92	(052-023-050)	CLINICAL	M SAVAGE MS

18-03-92	(052-023-054)	CLINICAL	M SAVAGE
20-03-92	(052-023-052)	CLINICAL	MS
23-03-92	(052-023-051)	CLINICAL	MS
26-03-92	(052-023-055)	CLINICAL	MS
02-04-92	(052-023-058)	CLINICAL	MS
07-04-92	(052-023-061)	CLINICAL	MS
13-04-92	(052-023-062)	CLINICAL	MS
16-04-92	(052-023-063)	CLINICAL	MS
16-04-92	(053-027-083)	CLINICAL	STAMPED DR SAVAGE & INITIALLED MS
27-04-92	(052-023-068)	CLINICAL	MS
12-05-92	(053-027-080)	CLINICAL	STAMPED DR SAVAGE & INTIALLED MS
14-05-92 & 15-05-92	(053-027-082)	CLINICAL	MS
17-05-92	(053-027-083)	CLINICAL	MS
25-05-92	(054-057-130)	CLINICAL	MAURICE SAVAGE
28-05-92 & 29-05-92	(054-057-131)	CLINICAL	MAURICE SAVAGE
01-06-92	(054-057-132)	CLINICAL	MAURICE SAVAGE
22-10-92	(054-057-142)	CLINICAL	SIGNATURE OBSCURED
24-11-92	(054-057-145)	CLINICAL	UNSIGNED
30-11-92	(054-057-148)	CLINICAL	MAURICE SAVAGE
04-12-92	(054-057-151)	CLINICAL	MAURICE SAVAGE
06-01-93	(054-057-150)	OUT PATIENT	UNSIGNED
23-02-93	(055-053-112)	OUTPATIENT	DR JM SAVAGE

26-02-93	(055-053-109)	CLINICAL	M SAVAGE
14-04-93	(055-053-116)	OUTPATIENT	DR SAVAGE/MS
15-06-93	(055-053-122)	OUTPATIENT	DR SAVAGE
27-07-93	(055-053-124)	OUTPATIENT	DR SAVAGE
19-08-93	(055-053-127)	CLINICAL	MS
03-09-93	(055-053-127)	OUTPATIENT	DR SAVAGE
02-11-93	(055-053-130)	OUTPATIENT	DR SAVAGE
19-11-93	(055-053-131)	CLINICAL	INITIALS OBSCURED
14-12-93	(056-037-085)	OUTPATIENT	MS
15-12-93	(056-037-084)	CLINICAL	MS
21-12-93	(056-037-084)	CLINICAL	MS
11-01-94	(056-037-087)	CLINICAL	M SAVAGE / MS
05-02-94	(056-037-086)	OUTPATIENT	MS
12-05-94	(057-102-178)	OUTPATIENT	MS
09-06-94	(057-102-179)	OUTPATIENT	MS
14-07-94	(057-102-179)	OUTPATIENT	MS
24-08-94	(057-102-182)	CLINICAL	MS
06-09-94	(057-102-185)	CLINICAL	MS
13-10-94	(057-102-186)	CLINICAL	MS
Dec 94	(057-102-187)	OUTPATIENT	MS
12-01-95	(057-102-187)	OUTPATIENT	UNSIGNED
Jan 95	(057-102-187)	CLINCIAL	M SAVAGE
23-01-95	(057-102-187)	CLINICAL	M SAVAGE

02-02-95	(057-102-188)	OUTPATIENT	UNSIGNED
02-03-95	(057-102-190)	OUTPATIENT	MS
13-04-95	(057-102-190)	OUTPATIENT	M SAVAGE
11-05-95	(057-102-191)	OUTPATIENT	MS
18-05-95	(057-102-191)	CLINICAL	MS
02-06-95	(057-102-192)	OUTPATIENT	MS
08-06-95	(057-102-191)	CLINICAL	MS
22-06-95	(057-054)	CASE NOTE/DISCHARGE SUMMARY	M SAVAGE
Nov 95	(058-012-037)	TRANSPLANT ON-CALL CHECK LIST	UNSIGNED
09-11-95	(058-035-143)	CLINICAL	UNSIGNED NOTE RE: DR WALFORD APPOINTMENT
13-05-92 to 09-11-95	(058-011-033 to 036)	INVESTIGATION SUMMARY SHEETS	UNSIGNED
17-08-95	(058-035-127)	CLINICAL	MS
14-09-95	(058-035-125)	CLINICAL	MS
25-09-95	(058-035-128)	CLINICAL	M SAVAGE
27-11-95	(058-035-133)	CLINICAL	M SAVAGE
27-11-95 (UNTIMED)	(058-035-138)	CLINICAL	M SAVAGE
27-11-95 (8.30pm)	(058-035-140)	CLINICAL	M SAVAGE
27-11-95 (11.00pm)	(058-035-140)	CLINICAL	M SAVAGE

Belfast Health and Social Care Trust

HEALTH AND SOCIAL CARE AUDIT IS:

"a quality improvement process that seeks to improve patient care and outcomes through systematic review of care against explicit criteria and the implementation of change."

Principles for Best Practice in Clinical Audit (2002, NICE/CHI)

PROCESS FOR AUDIT:

Need for audit identified by group within or across service areas.
Audit team identified, to include Consultant or Senior Manager.

↓

Complete & submit Audit Proposal form

↓

Proposal assured and registered with Standards, Quality & Audit Dept.
Project Lead contacted to agree time frame and any SQA Support Required

↓

Audit

↓

Develop & submit Action Plan

↓

Re-audit identified for that Service Areas audit plan.

Want HELP with an audit

Contact:

Standards Quality & Audit Dept. 4th Floor, Bostock House, RVH

Fintan McErlean:	fintan.mcerlean@belfasttrust.hscni.net	02890 636379
Julie McGrady:	julie.mcgrady@belfasttrust.hscni.net	02890 636785
Simon Dunlop:	simon.dunlop@belfasttrust.hscni.net	02890 636378

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

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

REF	Document
Q2d	Renal transplant On-Call Information booklet
Q18a	Clinical Paediatric Nephrology, 2nd Edition 1994 pp 111-117, Editor RJ Postlethwaite, Publisher Butterworth-Heinemann ISBN 0750613475)
Q18b	The Handbook of Neonatal Intensive Care, Halliday, McClure and Reid, Balliere Tindall 1989 (ISBN0-7020-1399-4)
Q36c	Paediatric Vade Mecum, page 207, 1989 by Edward Arnold, edited by J Insley
Q46a	Protocols
	The Royal Manchester Children's Hospital
	The Royal Free Hospital in London
	Guy's Hospital London
	Birmingham Children's Hospital
	UCLA
Q46c	Policy for the administration of IV fluids to children, The Belfast Health & Social Care Trust 2009
Q47a	DHSSPS Parenteral Fluid Guideline
Q49g	Audit (Postlethwaite RJ et al, Paediatric Transplantation 2002:6:367-377
Q54a	Viewpoint Article, lancet 2003; 362:1320-23
Q54a	The Standard Paediatric Textbook of Paediatrics, Forfar & Arneil 6th Edition 2003
	Standards and Guidelines Committee Policy of IV Fluids for children from 1 month-16th birthday, Revised April 2009)

Compiled by members of the

PAEDIATRIC RENAL UNIT
CITY HOSPITAL · NOTTINGHAM NG5 1PB

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Bordon Hants, from whom further copies can be obtained.

Kidney Transplantation in Childhood

A guide for families

contents

You may have already learnt some of the facts about kidney transplantation from the chronic renal failure booklet. This booklet gives more information about what happens before and after a kidney transplant.

why is a transplant necessary?

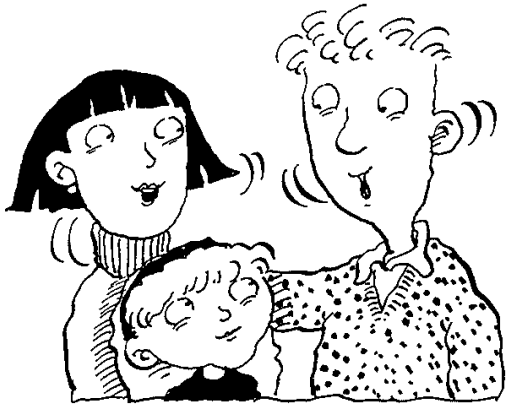
Dialysis is only a temporary measure before a kidney transplant becomes available. Even if dialysis is going well and keeping your child healthy, it is a renal transplant which offers the best quality of life. With a successful transplant there should be less disruption to family and school life. Diet and fluid restrictions should no longer be necessary.

Occasionally a kidney transplant may be considered before a child needs dialysis. This may be discussed with you by your kidney specialist (nephrologist) and transplant surgeon.

at what age do we consider a transplant?

There is no strict age limit but kidney transplants in infants are usually more difficult to manage.

where does the transplant kidney come from?



Most children receive a transplant from a person who has died in an intensive care unit and where the relatives have agreed to donate the kidneys. This type of transplant is known as a cadaveric kidney transplant.

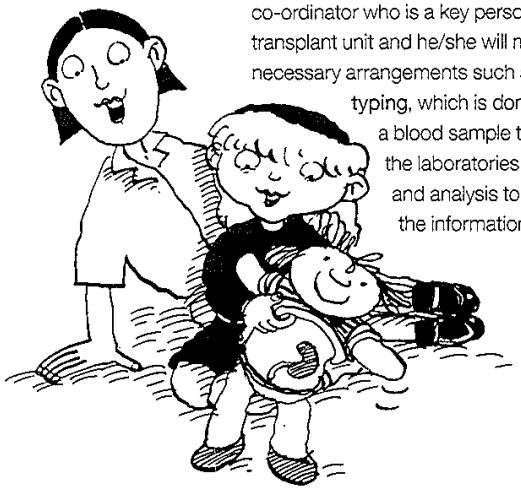
A kidney may also be donated by a family member. This is known as a living related donor transplant. For children this usually means a mother or father. As this type of operation involves operating upon a healthy individual, some units are reluctant to do this. If going ahead transplant surgeons require a detailed physical and social assessment.

Since most children will receive a cadaveric kidney transplant their name has to be added to the national transplant waiting list.

what assessment is necessary?

Placement on the **transplant waiting list** follows discussion with the kidney specialist and transplant surgeon. Preparation is very important for all the family and this will be carried out by the primary nurse and play leader. Visits to the area where your child will be nursed after the operation will be arranged. Play therapy using dolls, videos and photograph albums of other children who have undergone a transplant may be helpful.

The social worker will also meet with the family to discuss ethical issues and any other other problems which can be helped by discussion and information. It is important that your child's questions and fears are talked about as well as your own. You will also meet with the transplant co-ordinator who is a key person within the transplant unit and he/she will make all the necessary arrangements such as **tissue typing**, which is done by taking a blood sample that is sent to the laboratories for processing and analysis to give most of the information required.

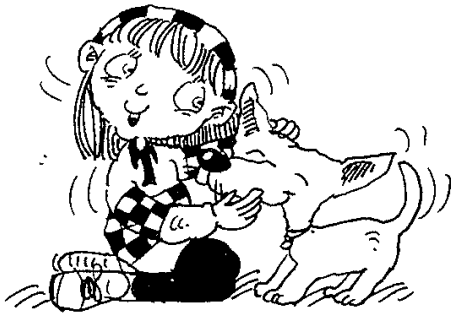


how are kidneys matched for transplantation?

To be offered a kidney your child has to be of a similar **blood group** to the donor. We also aim to match the **tissue type** (or genetic make up) of the donor and your child (the recipient). The level of **antibodies** in your child's blood is also important.

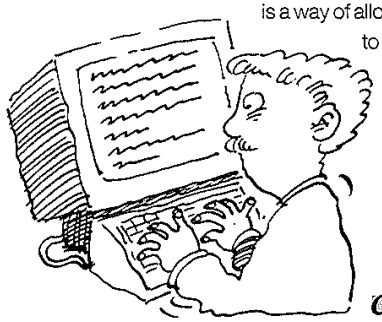
what are antibodies?

We all have antibodies in our blood which can react against certain cells or tissue types. If your child has had previous transfusions or a previous transplant, then the level of antibodies in the blood may be high. A high level of antibodies means that it may take longer to match a suitable kidney. While on the waiting list your child's antibody levels will be checked by a blood test at regular intervals.



when will the transplant happen?

There is a large waiting list for kidney transplants which is held on a national computer based in Bristol. This does not function on a 'first come first served' basis but is a way of allowing a suitable matched kidney to be found. When the match between a donor kidney and your child's tissue type is suitable then he/she may be offered the kidney at any time. However, sometimes the wait can be quite long.



cadaveric kidney transplant

The majority of children receive this type of transplant and it is the transplant co-ordinator who will first receive details. As a donor kidney may be available day or night you will be asked to leave a contact number if you are away from home. Pagers may also be provided to help you keep in touch with the hospital.

The operation can only go ahead if your child is well and not suffering from colds and other infections. You will be asked to come to the hospital as soon as possible as there are tests to be done before it is finally agreed for the operation to proceed.

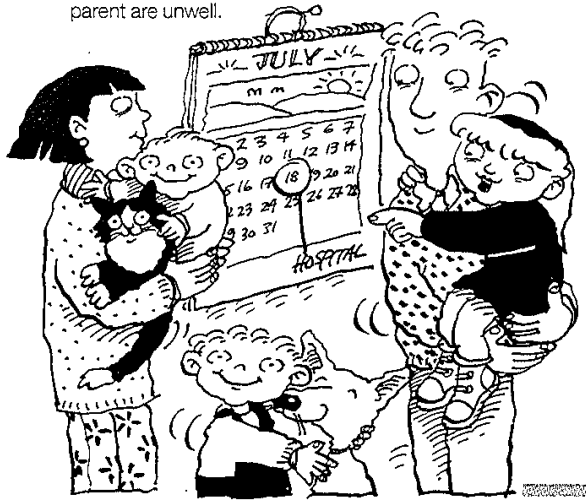
You can be assured that the donor is always tested for the HIV (AIDS) and other viruses. We always look carefully at the match and it is possible for children to have a kidney from an adult donor.

what does the transplant operation involve?

Routine blood tests and x-rays will be considered to make sure your child is fit for the operation. The operation may still be cancelled if the antibodies in your child's blood react against cells from the donor. This is what we mean by the term positive antibody crossmatch when it is inadvisable to proceed as severe early rejection can result.

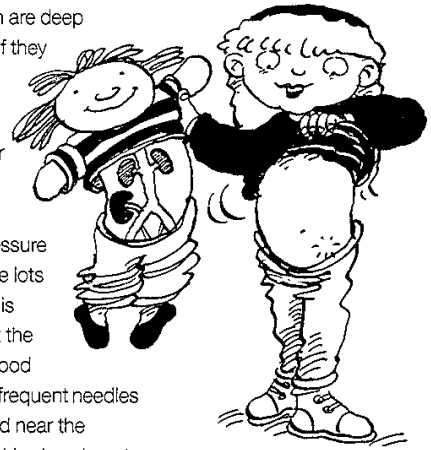
living related donor transplant

One of the major advantages of a living related donor transplant from a parent to a child is that the operation can be planned for a certain day and time. The parent will be in a theatre close to their child so that once the kidney is removed it can be placed straight into their child. The operation will be postponed if the child or parent are unwell.



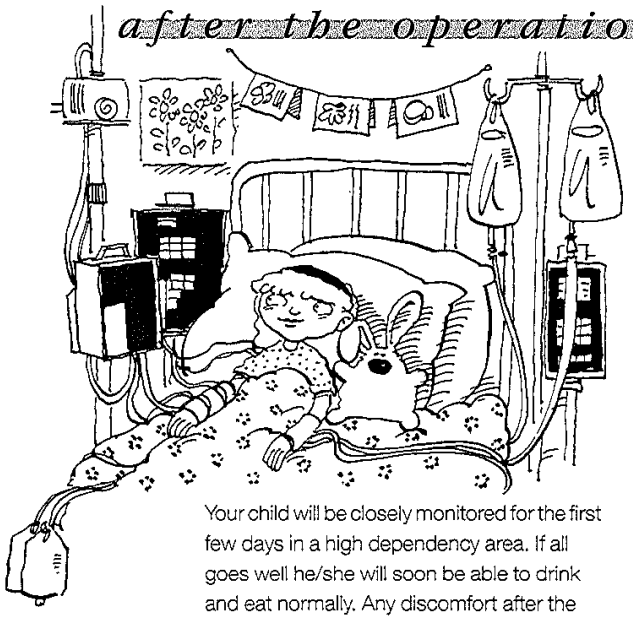
where is the kidney placed?

The transplant surgeon places the kidney low down in the abdomen to one side and usually outside the cavity containing the intestines and appendix. The appendix is not removed. The transplant kidney is placed low down on one side so that it can be joined to the major blood vessels going to the leg and also to avoid problems with the ureter leading to the bladder. The child's own kidney's which are deep in the back, are only removed if they are causing problems.



Before the transplant operation starts and while your child is asleep (anaesthetised) a tube is put into a large vein in the neck to measure the pressure in the veins and allow us to give lots of fluid quickly. Also a cannula is usually placed into an artery at the wrist which helps us to take blood samples without having to use frequent needles on your child. Drains are placed near the transplant and a tube (catheter) is also placed into the bladder to accurately measure the urine output. The reasons for all these tubes will have been explained to you and your child before the transplant happens. If your child is very worried about tubes and needles then we might ask the clinical psychologist to help us prepare your child. Some children also have a nasogastric tube placed down the nose to help us to drain fluid off the stomach until the bowels are again working.

what happens after the operation?



Your child will be closely monitored for the first few days in a high dependency area. If all goes well he/she will soon be able to drink and eat normally. Any discomfort after the operation will be controlled by an infusion of pain killers.

The drain from around the kidney will usually be removed after two to three days but the catheters into the bladder may stay in place for five to seven days. If there are signs that the kidney is not working then a special scan may have to be arranged. Sometimes transplants take some time to work properly and dialysis may be needed in the meantime. This can be a difficult and worrying time and all members of the renal team will keep you closely informed of progress. Hopefully the transplant will work well.

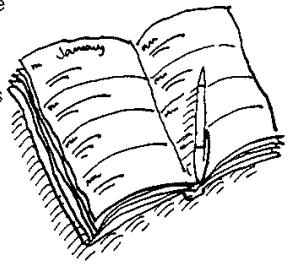
how long will my child be in hospital?

This will depend upon how your child recovers from the transplant operation. It may be ten days to several weeks depending upon how long the kidney takes to start working and whether there are any problems with rejection. Parents will be welcome to stay throughout this time. We appreciate that you may feel torn between your child in hospital, work and other family at home.

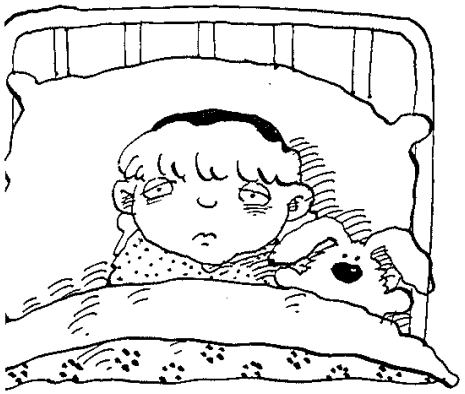
going home after the transplant

Before you are allowed home you will have some further teaching so that you can carry on monitoring your child's progress at home.

To begin with you may be asked to take your child's temperature, and measure the blood pressure and weight. You may be asked to record these along with the current drug treatment. Regular visits to the hospital will be necessary during the first few months so that your child's blood can be tested regularly as one of the most important signs of rejection is a rise in the creatinine level.



what is rejection?



Rejection is the term used for an attack on the kidney by the body's own defences. Signs may include fever, reduced urine output, tenderness over the kidney, rise in blood pressure and feeling generally unwell. If rejection is suspected then a biopsy of the transplant kidney may be needed.

how is a biopsy performed?

Using sedation so that your child does not feel any discomfort, a needle is placed into the kidney after an ultrasound scan has been performed. The tissue obtained can be examined under the microscope and can reveal what is going on within the kidney. This may be important information in the choice of treatment.

what drugs are used to prevent rejection?

Powerful drugs known as **immunosuppressives** are given in big doses at first and then gradually reduced with time.

Such drugs include **azathioprine, cyclosporin** and **prednisolone (steroids)**. The steroids used are corticosteroids and not the anabolic steroids abused by some athletes. Many units use a combination of all three and occasionally stronger drugs such as antilymphocyte or antithymocyte globulin or OKT3 may be necessary.

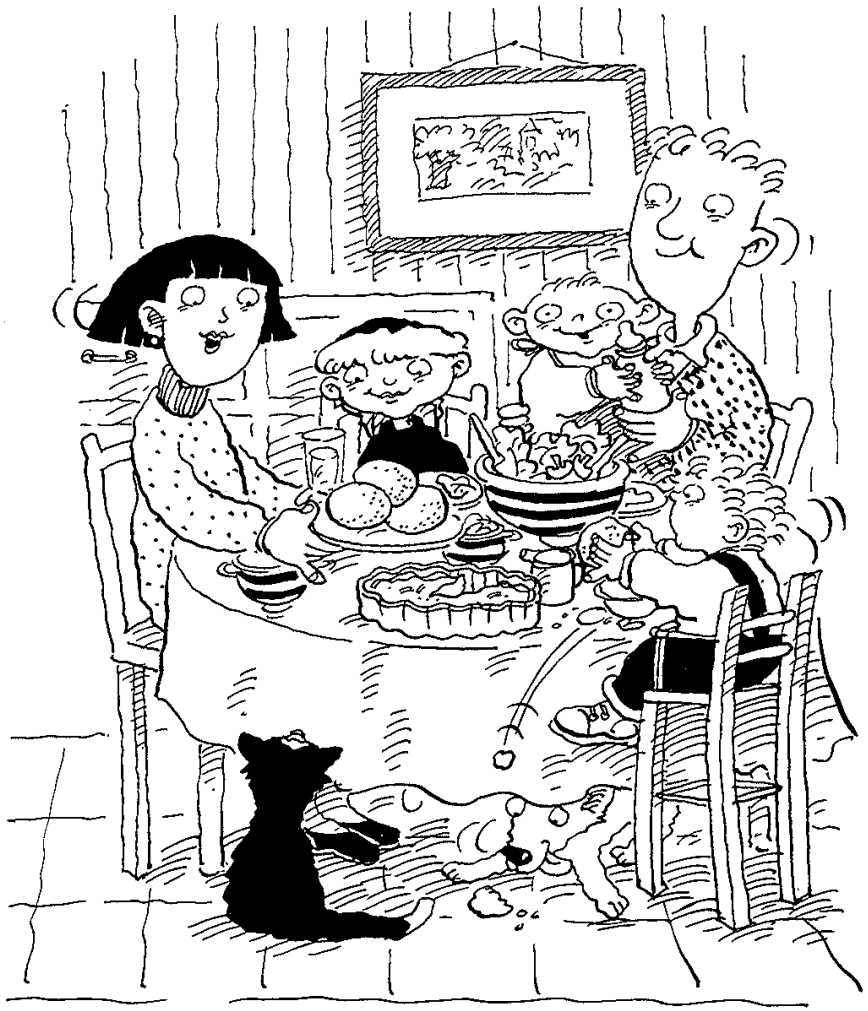
You should be aware that immunosuppressive drugs are taken for as long as the transplant kidney functions. It is important that drug dosages are not missed, although a few hours delay in the dose is not crucial.

how long will the transplanted kidney last?

Unfortunately kidney transplants do not last for ever. However some adult patients have had their transplants for over twenty years. It is possible to return to dialysis if the kidney fails, to await a further transplant.

Is there a special diet after transplantation?

One of the great benefits of the transplant is that your child is likely to have a better appetite, and diet and fluid restriction should be no longer necessary. Those children who required supplements or overnight feeding beforehand should start to eat and drink again. Weight gain can be a problem after the transplant, especially as appetite is increased by steroids. A 'no added salt' diet is still recommended to help control hypertension. A healthy eating diet will be encouraged for all the family.



physical changes after transplantation?

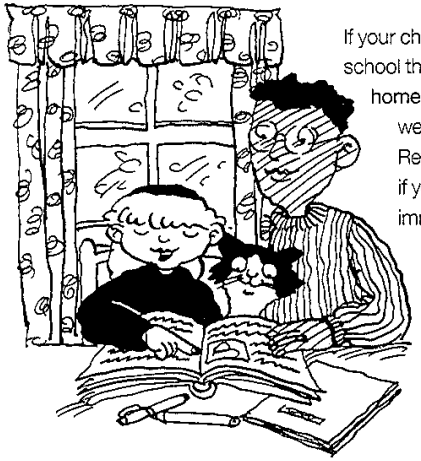
Initially weight gain and some fattening of the face is quite common but should improve after the steroid drugs are reduced with time. Cyclosporin may cause increased hair growth (called hirsutism) which may need treatment if it is embarrassing. Steroids can also cause an increase in spots or acne in the older child. Enlargement of the gums may also occur and your child should continue to have regular dental supervision. Always ask for advice if there is a problem.

removal of dialysis catheters after transplantation

These tubes are usually removed about two to three months after a successful transplant. The procedure can usually be done as a day case admission under general anaesthetic.

emotional well being

This is a period of great change in all your lives. Hopefully your quality of life will be greatly improved. However, there will also be a period of recovery from this stressful time. Your child may experience bad dreams and changes in behaviour which are all normal reactions and parents may feel exhausted.



If your child has lost some time off school then we will try to arrange a home tutor during the first few weeks after a kidney transplant. Return to school may be delayed if your child is on high doses of immunosuppressive drugs which make them susceptible to infection. As there may be some problems with school adjustment, team members will visit the school to explain the treatment and offer a supportive link.

Members of the renal team are always available to give you advice and support after the transplant. If the transplant is successful there will be a reduced contact with the unit compared to the days when your child was on dialysis.

Many recipient families wish to send a letter of thanks to the donor family which is always well received. This may be written any time after the transplant operation. The letter usually expresses sympathy, thanks and a brief description of the child pre and post-transplant. First names may be used but the letters should remain anonymous with no surnames or addresses. The transplant co-ordinator will arrange postage and she/he or other team members are always willing to help you write such a letter.

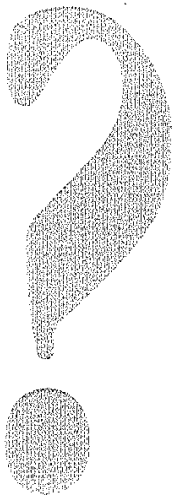
are my child's activities restricted after a transplant?

We encourage as much physical exercise as possible. However we do caution against a few sports such as rugby or martial arts as the kidney may be vulnerable to direct kicks or blows.

Your child can go swimming after the dialysis catheter and/or feeding tube is removed.

Every year there is a national event called the Transplant Games where children and adults who have had organ transplants compete. Your child is welcome to participate.

common questions



1. Can we travel or go on holiday when we are on the transplant list?
YES. However, it does need to be discussed and planned with the renal team.

2. After the transplant, how far can we go away on holiday?
If the transplant goes well, then after about three months a holiday anywhere in the UK could be planned. However, it will depend upon how frequent your child needs to be checked and whether we can make local arrangements for blood tests or check ups if these are necessary. Holidays abroad are also possible but should be deferred until it is certain everything is going well with the transplant.

3. Should seat belts be worn in the car?
Although the lap portion of the seat belt may press slightly over the transplant area this does not harm the kidneys. The wearing of seat belts is compulsory and always recommended.

4. Vaccinations and immunisations
When your child is taking immunosuppressive drugs then all live vaccines such as BCG (for tuberculosis) and live polio should be avoided. Vaccines made from dead bacteria may be acceptable, but always check with your nephrologist.

5. Which infections are a worry post-transplant?
Any infection after a transplant can be a problem but chicken pox is the major concern. If your child is a close contact such as a classmate sitting close by, then you should inform your GP and the renal unit. If your child develops chicken pox while on immunosuppressive treatment then get in touch straight away so that we can start treatment early.

6. What about drugs prescribed elsewhere after a transplant?
There are some antibiotics and other medications which can interact with Cyclosporin. If drugs are prescribed by other doctors then please check with the renal unit.

7. What if my child has sickness and diarrhoea?
These can interfere with the absorption of drugs into the body. If your child is improving during the day then the drugs can be given at a later time. If your child cannot keep any drugs down all day then please contact the unit for advice. If your child vomits back his/her tablets within an hour of taking them then the drugs should be given again.

8. Benefit changes?
Social Security benefits to which you are entitled will change post-transplant? It is best to seek advice from the social worker as the circumstances for each family and child is different.

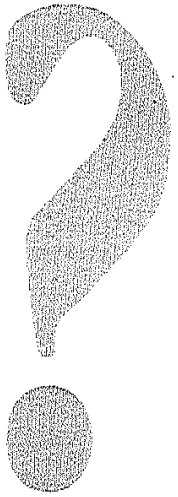
9. What do we tell the children about where the transplant kidney came from?
This sensitive question will need a sensible answer and is best discussed with team members.

10. Can my child have children in the future after the kidney transplant?
If the transplant is working well and your child enters adulthood with good health and good kidney function then it is possible for them to have children of their own. Contraceptive advice should be sought at the appropriate time. Use of the 'pill' must always be discussed with the nephrologist.

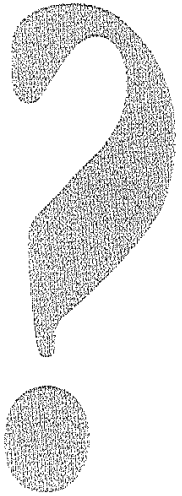
11. If my child has appendicitis post-transplant is there risk to the transplant kidney?
Not usually.

12. Are there precautions regarding skin care?
As the immunosuppressive drugs increase the sensitivity of the skin to the sun's harmful effects, avoidance of over-exposure to the sun and the use of sun block creams and hats is strongly advised. There is an increased risk of skin cancer in post-transplant patients and all suspicious moles or warts should be reported to the doctor.

13. Does my child require antibiotic cover for teeth extraction?
Please discuss this with your nephrologist.



useful terms



Antibodies – Proteins in the blood stream which react against foreign substances.

Artery – Blood vessel which carries blood away from the heart to the organs of the body.

Biopsy – Removal of a tiny piece of kidney tissue for special examination under a microscope.

Bladder – The sac which holds urine before it is passed out of the body.

Blood group – The type of blood you have, i.e. groups A, O, AB, B.

Cadaveric donor – A kidney donor who has died.

Cannula – Small plastic tube inserted into a blood vessel.

Creatinine – Waste product in the blood stream which is removed by the kidneys. Measuring the level tells us how well the kidneys function.

Cross matching – Test which matches your child's blood against cells from the donor.

Hypertension – High blood pressure.

Immunosuppressive drugs – Drugs given to damp down the body's response to the transplant kidney and prevent rejection. Azathioprine, Cyclosporin and Prednisolone (steroids) are the drugs commonly used.

Intravenous infusion – Fluid given through a cannula (commonly known as a drip).

Living related donor – Kidney donor who is a living relative of the child.

Primary nurse – The renal nurse who co-ordinates your child's care.

Recipient – Child who receives a kidney transplant.

Rejection – Vigorous response of the body's own cells to the kidney transplant. Methylprednisolone. Antilymphocyte Globulin (ALG), Antithymocyte Globulin (ATG) and OKT3 are strong drugs used to treat rejection.

Tissue type – Proteins on the surface of cells which define our individuality.

Ureter – Tube which carries urine from the kidney to the bladder.

Urinary catheter – Tube which drains urine from the bladder.

Vein – Blood vessel which carries blood away from the organs back to the heart.

18a

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[Insensible water loss − (Water of oxidation + Preformed water)] + Measured urine volume

Maintenance electrolyte requirements

Obligatory electrolyte loss is small and the kidney has a wide range of latitude in electrolyte excretion. It is the aim of normal maintenance, therefore, to provide an amount (Table 10.2) which will neither induce maximal renal conservation nor require excretion or a large unwanted excess. Electrolyte deficits are seen mainly in association with excess gastrointestinal or urinary loss, but sweating may also lead to considerable loss of electrolytes.

When treating infants and children with very large electrolyte deficits, the daily requirements are essentially negligible and may be disregarded. If parenteral fluid therapy is conducted over a relatively short period, the need for calcium, phosphate and magnesium supplements is negligible unless there are documented abnormalities in the plasma levels of these electrolytes. If the infant or child subsequently requires total parenteral nutrition, full electrolyte replacement will be necessary.

Disorders of sodium and water balance

Introduction

Disturbances of sodium and water balance are a frequent occurrence in paediatric clinical practice, both as primary and secondary manifestations of disease processes. Dehydration is a well-accepted but inaccurate term used to describe situations in which invariably there are combined water and electrolyte deficits, and in practice is used interchangeably with saline depletion.

The evaluation of a water deficit is by necessity a clinical one (Table 10.3), and in practice the accuracy of the evaluation reflects the experience of the clinician.[5]

In addition there is a tendency for inexperienced clinicians to equate changes in plasma sodium with changes in total body sodium status, e.g. a low plasma sodium is automatically assumed to indicate sodium deficiency and treated with the administration of saline. Interpretation of changes in plasma sodium requires information on the presence or absence of a fluid deficit and in particular assessment of the effective intravascular volume.

Table 10.3 Symptoms and signs of ECF volume contraction

Symptoms
Thirst
Restlessness
Confusion
Signs of reduced interstitial fluid (dehydration)
Dry mouth
Sunken eyes
Loss of skin turgor
Sunken fontanelle
Signs of reduced intravascular volume (hypovolaemia)
Increased core peripheral temperature difference
Poor peripheral venous filling
Tachycardia
Oliguria
Low central venous pressure
Hypotension
Peripheral circulatory failure

Urinary electrolyte (sodium and chloride) concentrations are of value, particularly in the patient with an obvious fluid deficit and also as confirmation of a low effective intravascular volume in patients with expansion of the ECF, e.g. cardiac failure, hepatic failure and nephrotic syndrome.[6]

A word of warning, however, is necessary against the slavish use of urinary electrolyte measurements, since both random measurements and excretion rates generally reflect intake.

The evaluation of the patient with a complex fluid and electrolyte problem not only requires serial biochemical monitoring, but equally importantly serial clinical evaluation, body weight and sodium and water balance recordings. It must be stressed that it is the combination of these clinical and biochemical data which allows successful management.

Hyponatraemia

Pure sodium deficiency is very rarely observed in paediatric practice, the occurrence in association with a fluid deficit being the norm. In the presence of sodium deficiency, a reduction in ECF volume is invariably present and the symptoms and signs reflect this (Table 10.3).

Complex classifications of hyponatraemic states may be produced (Table 10.4) but are unhelpful in assessing the clinical problem. It is intended here to give some practical guidelines on the assessment of hyponatraemic states

Table 10.4 Causes of hyponatraemia

Factitious hyponatraemia
Hyperglycaemia
Impermeant solutes:
- Mannitol
- Ethylene glycol
- Alcohol
- Methanol

Pseudohyponatraemia
Hyperlipidaemia
Hyperproteinaemia

True hyponatraemia
1. Loss of sodium in excess of water
   - Gastrointestinal loss:
     - Diarrhoea
     - Vomiting
     - Aspiration
     - Fistulae
     - Stoma
   - Skin loss:
     - Heat stress
     - Cystic fibrosis
     - Adrenal insufficiency
   - 'Third space' loss:
     - Thermal injury
     - Intestinal obstruction
     - Ascites
     - Muscle trauma
   - Renal loss:
     - Osmotic diuresis
     - Diuretic therapy
     - Post-obstructive diuresis
     - Recovery phase of ATN
     - Salt-losing CRF
     - Renal tubular disorders
   - Adrenal disease:
     - Congenital and acquired adrenal insufficiency
2. Gain of water in excess of sodium
   - SIADH
   - Excessive water intake
   - Glucocorticoid deficiency
   - Hypothyroidism
   - Antidiuretic drugs
   - Reset osmostat
   - Oedematous states:
     - Nephrotic syndrome
     - Hepatic failure
     - Cardiac failure
   - Renal failure

without necessarily being comprehensive (Figure 10.2).

Prior to undertaking the assessment of hyponatraemia it is important, first, to ensure that the blood sample has not been improperly drawn, e.g. at a site proximal to a hypotonic saline or dextrose infusion, and secondly to measure the plasma osmolality. The plasma osmolality may be high, normal or low (Figure 10.2).

Factitious hyponatraemia

Factitious hyponatraemia occurs as a result of fluid shifts between the ICF and ECF compartments due to the presence of abnormal relatively impermanent solutes in the ECF compartment. Examples of such solutes are glucose, mannitol or low molecular weight toxins, e.g. alcohol, methanol and ethylene glycol. In factitious hyponatraemia, the measured plasma osmolality is high despite the low plasma sodium and, with the exception of hyperglycaemia, the deficit between the measured and calculated plasma osmolalities will be > 10 mosm/kg.[7]

Pseudohyponatraemia

Many clinical biochemical laboratories report plasma sodium concentrations in mmol/litre of plasma and not in mmol/litre of plasma water. If there is an increase in the non-aqueous phase of plasma, as in hyperlipidaemia or hyperproteinaemia, the reported sodium concentration will be artificially low. The aetiology of the hyponatraemia is usually obvious in these cases and if the protein or lipid is extracted, and the estimation repeated, the plasma sodium concentration will be normal. In pseudohyponatraemia, the measured plasma osmolality is usually within normal limits and the deficit between the measured and the calculated osmolalities will again be > 10 mosm/kg.[7]

True hyponatraemia

In this circumstance, the measured plasma osmolality will be subnormal (< 285 mosm/kg). This occurs when either there is a loss of sodium in excess of water or a gain of water in excess of sodium (Figure 10.2). In order to allow further evaluation, a clinical assessment of hydration and in particular of intravascular volume is essential (Table 10.3).

Loss of sodium in excess of water

Extrarenal loss

Gastrointestinal	– Diarrhoea Vomiting Fistulae Aspirate Ileostomies
Skin	– Excessive normal sweating (cystic fibrosis, adrenal insufficiency)
Third space losses	– Thermal injury Intestinal obstruction Ascites Muscle trauma, etc.

These conditions will all give rise to the classical signs of dehydration and hypovolaemia (throughout this discussion the term hypovolaemia is taken to indicate the presence of a reduced effective intravascular volume). The kidneys respond appropriately with production of a small volume of concentrated urine with a urinary sodium concentration of < 20 mmol/litre on a random sample, and frequently < 10 in the older child with normal renal function. In addition, the urine osmolality will be high, as discussed in Chapter 21. All the above conditions may result in isotonic losses, i.e. equivalent losses of sodium and water, and in this circumstance the plasma sodium will remain within normal limits (130–150 mmol/litre). In addition, the urine biochemical findings will remain unchanged.

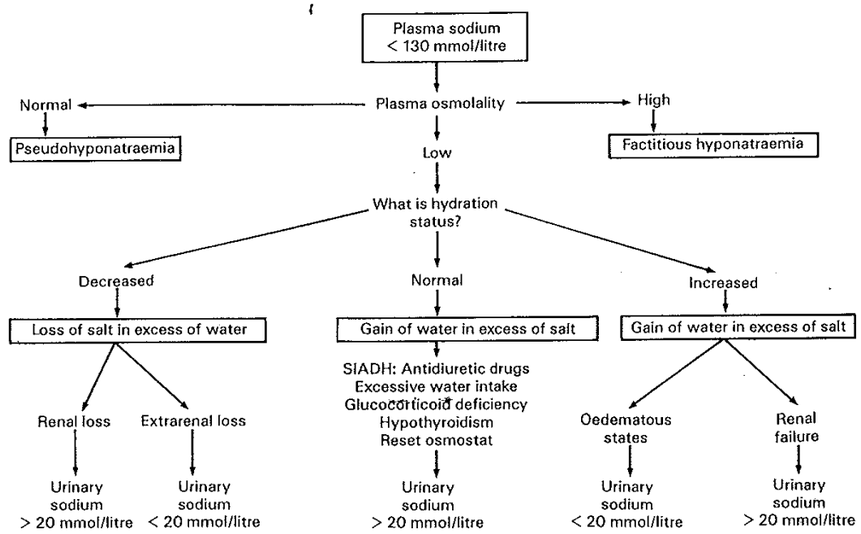

Figure 10.2 Assessment of hyponatraemia

Hyponatraemic states are increasing in incidence and now may account for up to 25% of infants with diarrhoeal dehydration.[8] The clinical signs of hypovolaemia/dehydration may present with a correspondingly smaller fluid deficit than in isonatraemic/isotonic dehydration. As well as the effect on ECF volume, the rapid drop in sodium concentration leads to a drop in ECF osmolality. If hypotonic replacement fluid is given, symptomatic water intoxication (see below) may occur despite the total body fluid deficit.[8]

Salt-losing states

Renal	– Osmotic diuresis Diuretic therapy Post-obstructive diuresis Recovery phase of acute tubular necrosis Salt-losing chronic renal failure Renal tubular disorders
Non-renal	– Mineralocorticoid deficiency/resistance

In the above conditions the clinical signs of hypovolaemia/dehydration will be present, but

Table 10.5 Causes of SIADH

CNS disorders
Infection
Malignancy, primary or secondary
Trauma
Hypoxic–ischaemic encephalopathy
Vascular accidents
Guillain–Barré syndrome
Cerebral malformation
Pulmonary disorders
Infection, acute and chronic
Malignancy
Cystic fibrosis
Positive pressure ventilation
Post-surgery
Anaesthetic or premedication
Abdominal, cardiothoracic and neurosurgery
Miscellaneous
Acute intermittent porphyria
Leukaemia
Lymphoma

the kidney will not respond appropriately. Urine sodium concentration remains high (>20 mmol/litre) and urine volume will be maintained to a relatively late stage, thereby enhancing the risk of significant salt and water loss. The association of hyponatraemia and significant hyperkalaemia should always suggest the possibility of adrenal insufficiency.

Gain of water in excess of sodium

Syndrome of inappropriate ADH secretion. Physiological regulation of ADH secretion involves both osmotic and non-osmotic stimuli.[9] In certain pathological states, continued secretion of ADH in the presence of ECF hypo-osmolality may either be appropriate, in the presence of non-osmotic stimuli, e.g. diminished intravascular volume, or inappropriate where no obvious stimuli are present. Since the initial description of the syndrome of inappropriate ADH secretion (SIADH), it has become clear that in some of the conditions in which it has been described (Table 10.5), notably malignant disease, ectopic production of ADH is responsible. In others, the mechanism remains unclear and the subject of ongoing debate.[10]

In SIADH, an increase in the ECF volume and reduction in osmolality fails to suppress ADH secretion and if normal fluid intake is maintained hyponatraemia develops. The sequence of events shown in Figure 10.3 will continue until a new equilibrium is achieved, when restoration of aldosterone secretion and decreased collecting duct permeability serve to limit the sodium loss and water retention, respectively. The term SIADH is frequently misused in clinical practice, since many examples of hyponatraemia may have an alternative explanation. It is therefore important that the following diagnostic criteria are followed:

- Hyponatraemia and hypo-osmolality.
- An inappropriately elevated urine osmolality. In the presence of reduced plasma osmolality, a maximally dilute urine (osmolality of < 100 mosm/kg) should be expected. A urine osmolality above this level should be viewed as inappropriate in the presence of reduced plasma osmolality. Urine osmolity therefore may be isotonic or hypotonic compared with plasma and still be considered inappropriately high in the context of this syndrome.
- Evidence of an increase in body water. This is usually shown by an increase in body weight rather than by overt oedema or a hyperdynamic circulation. It is perhaps best characterized as an absence of signs and symptoms of hypovolaemia/dehydration in the presence of hyponatraemia.
- Absence of other conditions which cause a retention of free water and hyponatraemia, e.g. renal, hepatic, cardiac failure or adrenal, pituitary and thyroid dysfunction.
- The absence of other known stimuli of ADH secretion, e.g. drugs, thermal injury, pain and nausea.

Additional findings are helpful but not essential:

- History of conditions associated with SIADH (Table 10.5).
- Decreased plasma urea and creatinine as a consequence of increased ECF volume and glomerular filtration rate (GFR).
- Urinary sodium excretion, as in normal subjects, is a reflection of sodium intake in these patients and the urine concentration is usually >20 mmol/litre, but shows a normal response to sodium restriction.

This variety of hyponatraemia may be acute or chronic and is primarily due to water retention in the absence of sodium retention, with the retained water being distributed equally between the ICF and ECF spaces. The symptoms of SIADH are predominantly neurological as a result of the increase in intracerebral water and rarely present until the plasma sodium falls below 120 mmol/litre, but may develop at higher levels of plasma sodium if the rate of fall has been rapid. The early signs are lethargy, irritability, leading to stupor and disorientation and later to convulsions, and signs of raised intracranial pressure.

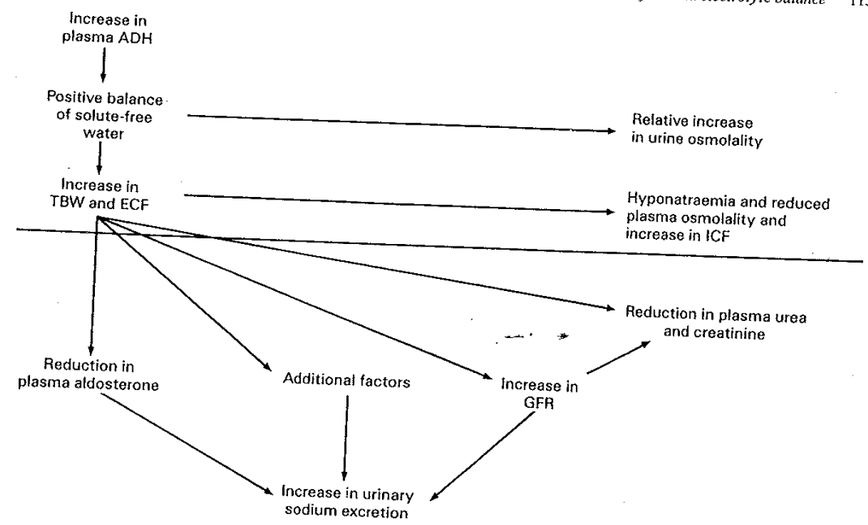

Figure 10.3 Mechanisms of SIADH. Events above the line are always present in this syndrome; events below the line usually but not invariably accompany the syndrome

Reset osmostat. Chronic, asymptomatic hyponatraemia may occasionally be seen in children with chronic infection or malnutrition. In these patients the level of ECF osmolality at which ADH is released is <285 mosm/kg.[10,11] Since these patients respond appropriately to both salt and water loading, specific therapy is not indicated.

Antidiuretic drugs. A number of drugs are capable of causing hyponatraemia secondary to renal water retention (Table 10.6).

Excessive water intake. Compulsive water drinking as a cause of hyponatraemia is rare in children. It is occasionally seen in adolescents, particularly girls with emotional or psychiatric disturbance. Other examples of excessive water intake occur with the use of hypotonic intravenous and oral fluid and enema therapy and following the absorption of water through the respiratory tract in patients treated with nebulized gas therapy or in a humidified atmosphere.

As with SIADH, the retained water is distributed between the ICF and ECF spaces so that oedema and hypervolaemia (cardiac failure, hypertension) are rarely seen. Symptoms again are neurological in severe cases. Urine volume will be increased in an attempt to eliminate the increased water intake, and urinary sodium excretion will reflect sodium intake (and the concentration will further be affected by the high urine flow). Urine will be maximally dilute (osmolality <100 mosm/kg). The haematocrit will be reduced, and both haemodilution and the increased GFR reduce the plasma urea.

Table 10.6 Drugs associated with hyponatraemia

Promote ADH release
Chlorpropamide
Clofibrate
Carbamazepine
Vincristine
Vinblastine
Cyclophosphamide
Opiates
Histamine
Isoprenaline
Nicotine
Colchicine
Barbiturates

Potentiate ADH action
Chlorpropamide
Tolbutamide
Phenformin

Impair renal water excretion independent of ADH
Oxytocin
Thiazide diuretics

Oedematous states. In the nephrotic syndrome and in patients with hypoproteinaemia secondary to malnutrition, the reduction in plasma oncotic pressure allows a movement of fluid from the intravascular to the interstitial space. This reduction in effective circulating volume produces an increase in renal tubular reabsorption of sodium and water by a variety of mechanisms. This may be viewed as an attempt to correct the hypovolaemia, but because of the reduced plasma oncotic pressure the sodium and water retention leads to an expansion of the interstitial space and the production of oedema. Other oedematous states such as hepatic and cardiac insufficiency act through similar mechanisms consequent upon on a reduction in the effective intravascular volume.[12] Hyponatraemia develops in these conditions if more water than sodium is administered. Provided that the renal function is normal, the kidneys will respond appropriately, producing small volumes of concentrated urine with a urine sodium < 20 mmol/litre.

Renal failure (*with salt and water retention*). Salt and water retention may occur in both acute and chronic renal insufficiency. In the presence of a hypo-osmolar intake, more water than sodium will be retained, resulting in hyponatraemia. Retention of sodium and water results in expansion of the ECF, so that oedema and hypervolaemia dominate the clinical picture. The urine volume is usually reduced and the urine sodium concentration will be > 20 mmol/litre. Urine osmolality will be similar to the plasma osmolality which should be maintained despite the hyponatraemia, because of the elevation in the plasma urea.

Therapy of hyponatraemia

The management of hyponatraemia is dependent on the severity and duration of the hypotonic state as well as on the underlying pathogenesis. It is beyond the scope of this review to describe in detail disease-specific therapies, but a summary of the approach to the correction of hyponatraemia based on the above diagnostic categories will be outlined.

When considering therapy of extrarenal losses of salt and water and salt-losing states of renal and non-renal origin, it is useful to realize the extent of the sodium as well as the fluid deficit. The sodium deficit may be approximated in the following manner:

(140 − Plasma sodium) × 0.65 × Body weight in kg

As clinical evidence of hypovolaemia develops early in hyponatraemic dehydration, a resuscitation phase is commonly required and the fluid should be given as plasma or isotonic saline at a volume of 20 ml/kg over 30–60 min. If the possibility of a hypoadrenal state is considered, intravenous hydrocortisone should be given concomitantly with the intravenous fluid replacement. When the resuscitation phase has been completed, the fluid deficit should be replaced with 0.9% saline and the maintenance fluids should be appropriate to the age of the child. The aim should be to achieve the correction of the fluid and sodium deficit within a 24 h period. Throughout the period of rehydration, routine clinical monitoring should be carried out, in particular of urine output and weight, and potassium replacement given when the urine output is satisfactory.

In the infant who is not shocked and able to tolerate oral fluids, the use of an oral rehydration solution is justified. The deficit replacement solution should contain 60–90 mmol/litre of sodium and the maintenance fluid, 40 mmol/litre of sodium.

Hyponatraemia in the presence of clinically obvious fluid overload should be treated primarily by salt and water restriction with diuretic therapy. In hypoproteinaemic states, in order to preserve the intravascular volume a concomitant infusion of salt-poor albumin may be advisable. Guidelines on the management of salt and water retention in renal failure are given in Chapters 21 and 22.

The management of water retention in SIADH is related to the severity of the neurological symptoms and the basis is the creation of a negative water balance at the same time as attempting to remove or correct the underlying cause of the impaired water excretion. In an asymptomatic patient, water should be restricted to 25% of daily maintenance requirements. If severe water restriction is not successful, intravenous loop diuretics may be used in order to increase free water excretion. Sodium and potassium losses in the urine should be measured and replaced while holding water replacement to a minimum.

When symptoms of water intoxication are present, the objective is to correct the severe cerebral overhydration. This may be accomplished by rapidly increasing the effective osmolality of the ECF by the use of mannitol or hypertonic saline either alone or in combination with loop diuretic therapy. Plasma electrolytes must be monitored frequently during this phase of therapy and urinary electrolytes should be measured and replaced in a low volume of intravenous fluid as above.[13] If the syndrome of inappropriate ADH secretion is felt to warrant prolonged therapy, certain pharmacological agents may be considered, e.g. lithium or demeclocycline.

Attention has been focused in recent years on the possible relationship between the treatment of patients with hyponatraemia and water retention and the neurological outcome. Concern exists that some patients, particularly those with chronic hyponatraemia, do well initially and then suddenly develop significant neurological deterioration leading to death or permanent sequalae. Brain histology in fatal cases shows both central pontine myelinolysis and demyelination of extra pontine myelin-bearing neurons.[14] In a typical case, fluctuating levels of consciousness, behavioural disturbances or convulsions are the prodromal signs. Despite some experimental data supporting the relationship of this complication to the rapidity of correction of the hyponatraemia there are few clinical data, especially in children, to support this notion.

However, in view of the possibility that the correction of the hyponatraemia is responsible for demyelination, it would seem sensible first in symptomatic patients, after the plasma sodium has been corrected to approximately 125 mmol/litre, and secondly in asymptomatic patients, to aim for a slow correction over 24–48 h.[15]

Hypernatraemia

Hypernatraemia is by definition a plasma sodium > 150 mmol/litre. It reflects a deficiency of water relative to salt, but importantly does not reflect total body sodium which may be high, normal or low.

Since sodium is the principal extracellular osmole, hypernatraemia leads to hypertonicity of the ECF. The volume of this compartment is therefore relatively well maintained and the intracellular compartment bears the brunt of the fluid deficit. The classical signs of dehydration/hypovolaemia are therefore relatively less evident for any given fluid deficit. The physiological responses to hypernatraemia are first an increase in ADH secretion when the plasma osmolality increases above 285 mosm/kg. If the plasma tonicity remains high, despite ADH secretion, the second and more important response mechanism – that of thirst – comes into play. The awake and alert patient will then increase his water intake to order to maintain normal ECF tonicity.

There are several conditions (Table 10.7) but only two major mechanisms which result in hypernatraemia (Figure 10.4):

- loss of water in excess of sodium.
- gain of sodium in excess of water.

Loss of water in excess of sodium

Extrarenal loss
Gastrointestinal
Hyperventilation
Pyrexia

The commonest presentation of hypernatraemia in clinical practice is in association with a fluid

186

Handbook of Neonatal Intensive Care

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Third edition

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Preface to the Third Edition

Another 4 years have elapsed between editions of this handbook, and in this time considerable developments have occurred necessitating changes in our text. On the medical politics front the Report of the Royal College of Physicians on 'Medical Care of the Newborn in England and Wales' has helped to highlight deficiencies in services for the newborn and set down guidelines for improvements.

Medical advances include the greater evaluation and usage of surfactant replacement therapy for babies with respiratory distress syndrome, and the improvements in non-invasive imaging techniques discussed in detail in the second edition. AIDS has been a new and unwelcome problem and we have devoted a section to its effects on perinatal care. Because of advances in paediatric subspecialities we have asked our colleagues to review some chapters and our thanks are due to Dr Angela Bell for improving Chapter 16 (Neurological Problems); Dr Brian Craig (Chapter 17, Cardiovascular Problems); Dr Maurice Savage (Chapter 19, Genitourinary Problems); and Dr Dennis Carson (Chapter 20, Metabolic and Endocrine Problems).

Equally as important is a nursing input for a handbook such as this and we have encouraged Sisters Sheila Lamont and Phil Farrell to write short notes on nursing aspects of management at the end of most chapters. We hope that this innovation will increase the appeal of the handbook, whose aim remains to assist junior medical staff and nurses who care for ill and preterm babies.

We remain indebted to Lynda Thompson and Florence Herbert for their secretarial help and to Brendan Ellis for his line drawings.

March 1989

Henry L. Halliday
Garth McClure
Mark Reid

Table 96. Causes of acute renal failure.

1. Asphyxia
2. Hypovolaemia, haemorrhage
3. Dehydration: loss of fluid, inadequate fluid intake
4. Trauma, especially obstetrical
5. Renal artery thrombosis or embolism
6. Septicaemia
7. Heart failure, especially PDA
8. Drugs and toxins: gentamicin, tolazoline, indomethacin
9. Disseminated intravascular coagulation
10. Renal agenesis, polycystic kidneys, renal dysplasia
11. Congenital nephrotic syndrome
12. Nephritis
13. Obstructive uropathy: urethral valve, ureterocele, systemic candidiasis

renal). If plasma (P) and urine (U) electrolytes and creatinine (Cr) are available the fractional excretion of sodium (FE (Na)) or the renal failure index (RFI) may be calculated as follows:

$$FE(Na)=(UNa/PNa)/(UCr/PCr)\times 100$$
$$RFI=(UNa)/(U/PCr)$$

In prerenal failure FE(Na) is 0.8 ± 0.6 compared to 4.8 ± 1.4 in established renal failure while RFI is 1.0 ± 0.2 in prerenal failure and 7.2 ± 1.3 in established renal failure. If doubt exists try transfusion of blood or plasma (15–20 ml/kg). Mannitol increases renal medullary blood flow if given early in renal failure and frusemide increases renal cortical blood flow. Their value in the management of acute renal failure of the newborn has *not* been proved.

Hyperkalaemia may need urgent therapy. Arrhythmias unusual unless serum level over 8 mmol/l. Emergency treatment: 1–2 ml/kg of 10% calcium gluconate intravenously over 3 min with ECG monitoring. Insulin 0.2 units/kg with 0.5–1 g/kg of glucose and acidosis corrected with small doses (1 mmol/kg) of sodium bicarbonate. Calcium polystyrene sulphonate 1 g/kg/day in 10% dextrose rectally (see also p. 177).

Management

Look for underlying cause (see Table 96). Treat infection, stop nephrotoxic drugs, e.g. gentamicin.

Fluid and electrolytes

Fluids ordered on a day-to-day basis: the previous day's urinary output plus insensible water losses, which are in term infant 20 ml/kg/day in first week and in preterm 40–50 ml/kg/day. Catheterize bladder to measure urine output accurately. Protein restricted if blood urea high (3 g protein is catabolized to give 1 g urea). Limit sodium and potassium intake to <0.3 mmol/kg/day. Correct hypoglycaemia, hypocalcaemia and acidosis.

Try effect (upon urine output) of 5 mg/kg frusemide. If response occurs then continue maintenance of 2 mg/kg 6 hourly. When diuretics fail dopamine infusion at 1 μg/kg/min may produce a diuresis by improving renal blood flow.

Dialysis

Only required in patients that cannot be managed conservatively by fluid balance and correction of metabolic abnormalities. Indications for dialysis are severe hyperkalaemia, metabolic acidosis or over-hydration with pulmonary oedema or congestive heart failure and intractable hypoglycaemia. Peritoneal dialysis is efficient because of the large peritoneal surface area/weight ratio and increased clearance of peritoneal urea and creatinine in newborn.

Technique of peritoneal dialysis. Under sterile conditions infant-sized peritoneal catheter (Pendlebury Neonatal Cannula-Medcomp) introduced percutaneously after injection of local anaesthetic. The dialysis fluid is delivered through a closed system (Paediatric Dialysis Set, Avon Medical R3370) in which a Y connection allows alternate filling and draining of the peritoneal cavity. The fluid should pass through a water bath to ensure delivery at 37°C.

Volumes of 30–50 ml/kg are instilled in 30–60 min cycles until biochemistry or oedema corrected. Commercial dialysis fluids (Dialaflex 61, Boots) have similar electrolyte composition to plasma except for absence of potassium. A glucose concentration of 1.36% is usually employed but may be increased to 3–4% if satisfactory fluid removal

36C

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(i) urine:plasma (U:P) urea $\geq 5:1$
(ii) U:P osmolality $\geq 1{\cdot}1:1$
(iii) fractional excretion of sodium $< 1\%$ (see page 264)

If oliguria (<200 ml/24 hours/m^2) persists after rehydration or the U:P urea and osmolality ratios are low, the patient should be given mannitol 0·75 g/kg as 20 per cent solution intravenously. If a diuresis does not ensue, the mannitol infused may cause hypervolaemia, and the JVP must be carefully monitored. At this point it must be assumed that renal failure is established, and management must be modified accordingly.

(ii) Established renal failure In many patients conservative management of fluid, electrolyte and nutritional needs may be all that is required until spontaneous recovery occurs. In other circumstances prompt dialysis may be life-saving. While progress should be reviewed at least twice daily, a decision to initiate dialysis is always better taken at the beginning than the end of a working day, bearing in mind the supply of trained nursing staff.

Salt and water requirements To maintain a steady state the fluid requirement will be the sum of:

(i) Insensible loss;
(ii) Gastro-intestinal loss;
(iii) Urine output.

Insensible loss amounts to 300 ml/m^2/day. In infants in whom accurate length measurement presents practical difficulties, an allowance of 15–17 ml/kg/day is a reasonable approximation. The allowance should be increased by 10 per cent for each 1°C of fever present, and at high ambient temperatures. It should be remembered that 50 per cent of insensible loss is respiratory, and this requirement should be proportionately reduced in children being ventilated with humidified air.

Gastro-intestinal and urinary losses should be replaced volume for volume, using a solution with an appropriate sodium concentration (see page 58). However, many patients with established renal failure will in practice have either plasma volume expansion, peripheral oedema, or both, in which case a further reduction of fluid intake will be indicated. *Such over-hydration may have caused dilutional hyponatraemia; an attempt to correct this by sodium supplementation is contra-indicated because of the high risk of precipitating left ventricular failure.*

While an accurate record of fluid balance is highly desirable it may be impossible to achieve, especially in young children, and

RMCH

MANCHESTER

RENAL TRANSPLANATATION

CHECKLIST ON ADMISSION OF A PATIENT FOR A RENAL TRANSPLANT.

a) History; note - function of native kidneys,
- urine infections,
- is native nephrectomy needed?
- recent contact with infectious diseases,
- type of dialysis, if any,
- is haemodialysis required pre-op?
- is CAPD catheter to be removed or left?

b) Examination; note - state of nutrition,
- state of hydration,
- blood pressure,
- height and weight,
- exit site appearance (CAPD & central catheters),

c) Investigation;-

Hb, WCC, Pl, PT, PTTK, TT

X-Match 1-3 units, (depending on patient size)

U & E, HCO_3, Creat, Ca, PO_4, Alk Phos

Albumin, Total protein, ALT

Save serum for virology, esp; CMV Hep B.

Cytotoxic antibodies, if requested by Tissue Typing, (5mls clotted to St Mary's tissue typing), blood for cytoxic antibodies may be required urgently for crossmatch with donor if a recent sample is not available.

MSU for culture

Urine for Na, K, Creat (To compare with post transplant)

C x R

d) Arrange haemodialysis if indicated.
Organise theatre, anaesthetist, and assistant for transplant surgeon

e) Intra-operative drugs.
The following must be available in theatre;-
Frusemide (2mg/kg); Mannitol (1g/kg);
Methylprednisolone (15mg/kg);

POST-OPERATIVE GUIDE

When the urine output is inadequate post transplant use the guide below to assist in your clinical managment.

	TEMP	GAP	CVP	BP	TREATMENT
1)	↑		↓	↓	Volume
2)	↑		↑	↓	Dopamine
3)	↑		↑	↑	Hydrallazine

Most patients can be managed without the use of any vasoactive drugs. If urine output is still poor after correction of vital signs try a stat dose of Frusemide 2 mg/kg. Do not repeat this if the response is poor of shortlived. Discuss with Consultant.

If urine output falls in association with haematuria consider renal vein thrombosis and discuss with Consultant.

If anuric/oliguric reduce Cyclosporin and commence Aziathioprine and steroids.

INVESTIGATIONS POST RENAL TRANSPLANT

a) Biochemistry/Haematology/Bacteriology;
Blood gases, U & E's, Glucose
Ca, Hb, Pl, Coag
Timed urine (4, 6 or 12 hours) Na, K, Creat and Urea

Day 1 & 2 (4-6 Hourly as indicated)

Day 3 onwards

U & E's, Creat }
Ca, PO, ALP, ALT, Alb, T.Prot } daily
Hb, WCC, Pl, Film }

Cyclosporin trough levels - daily over the first week.
- thereafter twice weekly.

MSU - twice weekly.

Overnight urine for protein/creatinine - twice weekly.

Urine & saliva for CMV - weekly.

Sample to St. Mary's tissue typing (for antibodies) once weekly.

Cytotoxic antibodies weekly

b) Radiology;
CXR - daily initially, then as indicated.
Hippuran renogram and ERPF - Days 1, 3 & 5 then at least twice weekly.
First pass high dose DTPA scan - as indicated.

IMMUNOSUPPRESSION FOR RENAL TRANSPLANT

Immunosuppression depends on category of patient being transplanted.

Category 1

1st graft ~~and patient over 5 years~~

Primary immunosuppression - Cyclosporin ~~alone~~ (keep levels 200-400)
1st rejection treat with Methylprednisolone for 5 days
2nd rejection treat with Methylprednisolone for 5 days and then oral corticosteroids

Decisions about ATG, other monoclonal antibodies and triple therapy will be made in individual patients on the basis of biopsy appearances and Consultants.

Category 2

1st graft and patient under 5 years.

All patients to start on Triple therapy with
Aziathioprine 1.5mg/kg od IVI
Prednisolone 1mg/kg od IVI
Cyclosporin (keep levels 50-150) 1mg/kg bd IV

Rejection treatment - Methylprednisolone for 5 days

Decisions about ATG, and other monoclonal antibodies will be made in individual patients on the basis of biopsy appearances and Consultants.

Category 3

Second or third graft

Decision about commencement with either Cyclosporin alone or triple therapy to be discussed with Consultant at time of transplant.

Rejection managed as indicated above.

POST-OPERATIVE MANAGEMENT FOLLOWING RENAL TRANSPLANATION.

After transplantation the patient will return to either the renal unit of to ICU.

LINES REQUIRED: Arterial line for BP
Central Venous line for CVP, Fluids, Triple lumen
Peripheral venous line for fluids
Urinary catheter

FLUIDS:

1. Arterial line; 0.9% saline with 1 unit/ml of Heparin at 2 mls/hr
2. CVP line; 5% Dextrose to replace insensible losses.
3. Central/Peripheral line; a) 0.45% saline, 5% Dextrose + ~~Kcl,~~ or,
   0.18% saline, 4% Dextrose + ~~Kcl~~
   b) Morphine infusion.
   c) Cyclosporin infusion
   d) Any other fluids or drugs

4. U.O - replace ml/ml c 0.45% Saline + 5% D

* Arterial line, CVP line, drugs total = insensible loss. Dextrose saline to replace urine output.

DRUGS:

a) Cyclosporin A; 3mg/kg/bd given over 12 hours, continuous infusions
1mg/kg/BD in TRIPLE IMMUNOSUPPRESSION.
Commence as soon as patient is passing urine.
Add appropriate dose to 0.9% saline
For patients on triple therapy reduce to 1 mg/kg bd over 12 hours.

b) Morphine; 0.025 mg/kg/hr through peripheral line.
0.5 x Wt of patient (kg as mg) diluted to 40 mls with Dextrose then run at 2 mls/hr.

c) Nifedipine (orally) - to be given to all patients (to prevent CyA toxicity.) 10-20 ~~micro~~ milligrams SR Nifedipine bd.

OTHER DRUGS: Other drugs that may be required include;

a) Dopamine; 0-5 micrograms/kg/min = renal perfusion dose.
0-20 micrograms/kg/min for hypotension
3 x Wt of patient (kg as mg) diluted to 50 mls.
Then 1ml/hr = 1 microgram/kg/min.

Wrigley Ward.

RADIATION DOSE TO RENAL TRANSPLANT CASES

While an individual investigation of renal function using radioiodine-labelled Hippuran results in a very small radiation dose to the patient, when a patient is investigated many times (as the transplant patients are) it is important to reduce the radiation dose as much as possible.

Even though the Hippuran we use is specially prepared for determination of ERPF and has less than 0.5 percent free iodide, calculation has shown that the thyroid still receives a moderate dose. Uptake of radioiodide by the thyroid gland can be blocked by the administration of pharmacological amounts of stable iodide. Studies in adults have demonstrated that 50 mg iodide (8 drops Lugol's solution) per day can suppress 24-hour uptake by as much as 95 percent. I recommend therefore that except where there is allergy to iodide (or any other medical contraindication) children be given stable iodide from the day before administration of the radioactive preparation for 5 days, according to the following schedule

Age	Iodide drops Lugol's solution per day
0 - 1 yr	1
1 - 2	2
2 - 6	3
6 -11	4
11 -14	5
14 -17	6
17 -20	7

The other critical organ is the bladder wall due to the accumulation of radioactivity in the bladder. I therefore also recommend that the patient be encouraged to drink plentifully after the end of the investigation, i.e. once the 40 min blood has been taken, and to pass water frequently. This will facilitate the removal of the radioactivity from the body.

Note that a renographic examination using the gamma camera requires of the order of ten times the amount of radioactivity as does a simple ERPF determination. It is therefore very important that the information to be gained from a renogram is carefully considered when making the request.

R J M Bennett
November 1986

INTRA - OPERATIVE (1/kg) 5mg/m pred. (5mg/kg/hr):
Removal of clamps — ~~1.2g~~ 1/kg mannitol & lasix 2mg/kg.
POST - OP — 1mg/kg CyA.

DRUGS

1.5mg ~~Mpred~~ Aza } 8am
1mg M pred }

No Antibiotic

Heparin - correct all hypercoagulable children when their value PT. or PTTs < 2/3 control 10iu/kg/hr. MAX 4/7

NO Dopamine routinely

NO Nifedipine ~~10-20 mg SL~~ routine.

No Frusemide routine
~~Hyper~~

Morphine 25 microgm/kg/hr

(~~approx 1500/kg~~.
Insensible losses = formula.
300ml/m² = surface area)

FLUIDS

Intra-operative 5-10 mmHg.
(Blood ? + Alb to keep Hb ≥ 10g/dl)
H.A.S. WCC filter
Saline - rarely use crystalloid !!
Never dextrose/saline.
Access. Triple lumen c/line subclavian 7fg.
IA line

Post op fluids. IA line } 0.9% 1iu/ml
CVP }
0.45%. 5%. Dextrose No KCl
Insensible loss.
CyA in 0.9%. others in Dextrose

Blood tests 4hly 24hrs
6hly "
12hly

Cyclosporin level.

b) Hydrallazine; 0.2-1.0 mg/kg stat followed by 0.2-1.0 mg/kg/hr as required.
5 x Wt of patient (kg as mg) diluted to 50 mls.
Then 2 mls/hr - 0.2 mg/kg/hr.

c) Frusemide; 2 mg/kg stat IV

d) Aziathioprine; 1.5 mg/kg/day as a single dose orally or IV.

e) Methylprednisolone; 15 mg/kg/day IV over 4 hours for rejection
1 mg/kg/day IV for triple therapy (bolus)

f) Prednisolone; 1-2 mg/kg/day, orally

g) ATG; See under "renal tranplant rejection".

IMMEDIATE POST-OPERATIVE MANAGEMENT

Monitor temperature gap (core to periphery), BP, CVP and urine output.

Try to maintain a) Temperature gap < 2 degrees centigrade
b) BP as appropriate for the individual child
c) CVP at 4-8 mmHg (5-10 cms H_2O)
d) Urine output

Initially urine output ought to be about 4 mls/kg/hour. Later it will fall to about 2 mls/kg/hour. Individuals vary greatly in their post transplant output. The main thing is to ensure that the patient continues to diureses over the first few days by keeping the circulatory volume full and replacing all losses.

Initial urine output after a transplant usually has a sodium of 60-90 mmols/l and so 0.45% saline is the most appropriate replacment fluid. Later this will need to be changed to 0.18% saline to avoid salt overloading the patient.

Dialysis patients, particulary those on CAPD, are often maintained in a state of volume depletion. To get an adequate diuresis and to maintain CVP post transplant they require large volumes of saline or plasma. Do not be afraid to give these. In CAPD patients PPF is the most appropriate volume expander as they usually have low serum albumins.

Royal Free

PROTOCOL FOR CADAVER RENAL TRANSPLANTATION IN CHILDREN AT RFH

A IMMEDIATE PRE-OPERATIVE MANAGEMENT

ADMIT TO RIDDELL WARD PRIOR TO TRANSFER TO RENAL TRANSPLANT UNIT

PRE OPERATIVE MANAGEMENT TO BE UNDERTAKEN BY PAEDIATRIC REGISTRAR/SENIOR REGISTRAR

CLINICAL EXAMINATION TO ENSURE FIT FOR SURGERY

IF NO DIALYSIS (HD OR CAPD) DECIDE WHETHER DIALYSIS IS REQUIRED PRE OP - INVARIABLY YES

INVESTIGATIONS

1. ELECTROLYTES, i.e. Sodium, Potassium, Calcium, Urea, Creatinine.

   (These tests will be undertaken either by the Renal Unit Lab Technician, Tel Ext 4135 or Air Call via switchboard.)

2. FULL BLOOD COUNT (Haematology Lab) + clotting screen

3. TISSUE TYPING (Renal unit lab Ext 4134)
   10 mls clotted + 10 mls citrated (bottles obtained from tissue typing laboratory)

4. CROSS MATCH 4 UNITS OF BLOOD (Blood transfusion)

5. CMV SCREEN - Blood, urine and mouth swab

6. CHEST X-RAY

7. PARENTAL CONSENT

8. INFORM ANAESTHETIST AND OPERATING THEATRE (Mr. Fernando's SHO and/or Registrar will usually arrange).

9. PRE MEDICATION IF INDICATED LIAISE WITH ANAESTHETIST

10. PRE OP IMMUNOSUPPRESSION - See Appendix B

11. 10 mls clotted blood, after at least 4 hr fast, for measurement of growth factor PLEASE CONTACT Dr Maxwell, bleep 006 or discuss with renal registrar on call.

B. IMMUNOSUPPRESSION

RECIPIENTS OF 1st GRAFT (CADAVER OR LIVE RELATED) WITH NO PRESENT OR PAST HISTORY OF CYTOXIC ANTIBODIES will receive:

A. Steroids
B. Cyclosporin A
C. Azathioprine

DOSES

A. Corticosteroids

PRE-OP 1 hour pre-op; 600 mg/m^2 Methyl Prednisolone i/v (use attached nomogram to calculate surface area).

POST-OP oral Prednisolone (or equivalent i/v) a 60 mg/m^2/day (two divided doses)
reducing to
10 mg/m^2/day (two divided doses) as primary graft function improves maintain this dose for 4 weeks,
then 5 mg/m^2/day (single daily dose) for 4 weeks
then
10 mg/m^2 alternate days.

B. Cyclosporin A

PRE-OP a) 1 hour pre op; 50 mg/m^2, i/v

POST-OP b) commence IV Cy A at 1.5 mg/kg/dose bd then adjust to achieve levels between 50 and 150 ng/ml.

Monitor levels daily (Renal lab)

C. Azathioprine

POST-OP 60 mg/m^2 as a single daily dose

Check previous drug regimen and in particular note whether the child has been on a beta-blocking drug. If so this should be discontinued and warn the anaesthetist that the child may need betasympathomimetic drive - best achieved by infusing dobutamine (dose between 2 and 10 µg/kg/min according to clinical response).

IMMEDIATE POST OPERATIVE MANAGEMENT

1. RETURN TO TRANSPLANT UNIT

2. SEDATION AND ANALGESIA (usually OMNOPON 0.1 mg/kg/i/v)

3. MONITORING

a) WEIGHT
b) PERIPHERAL AND CENTRAL TEMPERATURE
c) BLOOD PRESSURE
d) CENTRAL VENOUS PRESSURE
e) URINE FLOW

4. CHEST X-RAY - on return to check position of central venous line

5. CHECK - full blood count, creatinine, urea and electrolytes, bicarbonate, calcium.

Fluid management - a high urine flow rate is desirable (certainly over 2 ml/kg/hour). Replace urine output initially with half normal saline, volume for volume on an hourly basis. Check the urinary electrolytes and plasma electrolytes four hourly initially. Often some normal saline is necessary for replacement of urine volume to maintain a normal plasma sodium. If potassium falls a knowledge of the urinary potassium excretion rate is helpful in calculating replacement.

Anticipate hypovolaemia (low peripheral temperature, low CVP, tachycardia, BP may be low) and infuse colloids as rapidly as necessary to maintain a CVP of >5 cm of water. Use blood or plasma according to the haemoglobin.

Hypertension - it is common to see hypertension in the immediate post operative period. If the CVP is normal vasodilate with Hydralazine 0.3-0.5 mg/kg/i/v, to be repeated as necessary. Vasodilatation may also be achieved with Chlorpromazine 0.1 mg/kg/i/v.

C. AT OPERATION

1. INSERTION OF CENTRAL VENOUS CATHETER FOR CVP MONITORING DURING AND POST OP.

2. INSERTION OF PERIPHERAL VENOUS LINE

3. INSERTION OF ARTERIAL LINE FOR POST OP. MONITORING OF BLOOD PRESSURE AND BLOOD GASES IF INDICATED.

D. ANTIBIOTIC THERAPY

Cadaver graft recipients should receive:

1) Cefotaxime in standard paediatric dose. 1st dose to be given with the pre-med and continued until a negative culture has been obtained from the transplant transport fluid. Usually this means for 48 hours. Live donor graft recipients to be given antibiotics only according to specific indications.

2) Prophylaxis for pneumocystis with Septrin, 2 mg/kg as Trimethoprim component.

APPENDIX A

IMMUNOSUPPRESSION

RECIPIENTS OF 2nd OR SUBSEQUENT GRAFT (CADAVER) WITH PRESENT OR PAST HISTORY OF CYTOXIC ANTIBODIES will receive:

A. ATG
B. Steroids
C. Cyclosporin A
D. Azathioprine

A. ATG

PRE-OP 2 mg/kg I/v)
) For a total of 10 days
POST OP 2 mg/kg/day I/v)

B. Corticosteroids

PRE-OP 1 hour pre-op; 600 mg/m^2 Methyl Prednisolone I/v
(use attached homogram to calculate surface area).

POST OP oral Prednisolone (or equivalent I/v) a 60 mg/m^2/day
(two individual doses)
reducing to
10 mg/m^2/day (two divided doses) as primary graft function improves; maintain this dose for 4 weeks
then 5 mg/m^2/day (single daily dose) for 4 weeks
then 10 mg/m^2 alternate days.

C. Cyclosporin A

PRE-OP a) 1 hour pre-op; 50 mg/m^2, I/v

POST OP b) commence IV Cy A at 1.5 mg/kg/dose bd, then adjust to achieve levels between 50 and 150 ng/ml.

Monitor levels daily (Renal Lab)

D. Azathioprine

POST OP 60 mg/m^2 as a single daily dose from Day 7

HEPARINISATION DURING TRANSPLANTATION

All the dose schedules are given subcutaneously, the first soon after induction of anaesthesia:

>40 kg	5,000u bd
20-40 kg	2,500u tds
15-20 kg	1,500u tds
<15 kg	1,000u tds

Guys GUYS

TRANSPLANT WORK-UP PROTOCOL

1. **Blood group** needs to be taken when patient is being considered for transplantation.

2. Arrange a date with Lesley Kennedy, tel. 0171-955-4514 for **tissue typing.** (No tissue typing facilities on Fridays)

3. When sending blood for tissue typing **a copy of the blood group MUST** be sent with it (a photocopy is fine).
   As well as pages 1 and 2 in triplicate of the UKTSSA Recipient Registration Form, together with a South Thames Tissue Typing Form.

4. Bloods for

   HEP B
   HEP C
   CMV latex
   HIV

   need to be sent.

5. CXR
   ECG
   ECHOCARDIOGRAM
   and EXERCISE ECG need to be arranged

   Exercise ECG's for all patients over **50 years** old
   and
   ALL DIABETIC PATIENTS
   also
   If indicated by ECHO an Exercise ECG is to be arranged.

6. Results to go on computer as they are received please.

GUIDELINES FOR THE MANAGEMENT OF RECIPIENTS OF RENAL TRANSPLANTATION

Patients awaiting a renal transplant may be:-

a) On maintenance hospital haemodialysis
b) On peritoneal dialysis (CAPD)
c) At home with a failing transplant
d) Not yet on any form of treatment but have severely impaired renal function

Tissue typing is performed at the Regional Tissue Typing Laboratory at Guy's Hospital (Extension 4514). When a kidney becomes available, the Consultant Transplant Surgeon is informed of suitable recipients and with the Consultant Paediatrician will decide who shall be transplanted, based on matching criteria.

WHEN A KIDNEY BECOMES AVAILABLE

Transplant waiting list with names, addresses and telephone numbers is with the Paediatric Consultant on call. Tell the patient not to eat or drink anything more, if the transplant is planned immediately, and come to the hospital as soon as possible. Arrange the bed.

At this time the on-call SHO/Registrar will be informed as to which patient is to be transplanted. Patients belong to three broad categories:-

		Protocol
1	Non sensitized patients	A
2	Sensitized with negative cross match (cytotoxic and FACS)	A
3	Highly sensitized with positive cross match (cytotoxic and FACS)	B

The patients in the first two groups are transplanted with the same protocol A, but with group 2, there is a higher risk of early postoperative acute rejection.

TRANSPLANT PROTOCOL FOR SENSITIZED PATIENTS WITH NEGATIVE CROSS MATCH

A number of patients awaiting transplantation will have acquired HLA antibodies as a result of transfusions or failed transplants. All treatments are as for Treatment Protocol A but extra care must be taken in assessing these patients for any possible infection, rejection, etc. **3 times per week bloods to tissue typing are important for monitoring cellular and antibody responses.**

ALL PATIENTS ON ADMISSION:

Clinical history and examination; checking for infections, fluid overload, date of last blood transfusion etc.

Urea and electrolytes, creatinine, LFTs (profile 7)
Full blood count and platelets
Venous blood gas
Clotting screen
Group and X-match (2 units)
Tissue typing clotted blood 5 ml
Tissue typing heparinised blood (green topped tube) 5 - 10 ml
ECG and CXR
MSU - (if patient passes urine)
Tissue typing bloods - 5 ml in green topped tube
TENCKHOFF - send sample of peritoneal fluid and swab from exit site
CONSENT

Calculate body surface area from height and weight. Write them on prescription sheet and the clerking notes. Prescribe immunosuppressive drugs and fluids, pre- and postoperation.

For highly sensitized patients (group 3, protocol B) bloods must be sent to Guy's Tissue Typing Laboratory.

A. TRANSPLANT PROTOCOL A - FOR NON-SENSITIZED PATIENTS

If patient is on haemodialysis, check when last dialysed. If urgent dialysis is required contact on-call dialysis nurse.

If patient on CAPD, drain fluid out and cap off, **leaving abdomen empty.**

Before theatre:

ALG	0.2 ml/kg IV (pre-op and for 3 daily doses post-op). Give hydrocortisone 100mg IV (50mg if < 10kg) and chlorpheniramine 10mg IV (5mg if < 10Kg) 1 hour before ALG infusion. Give a test dose 0.1 - 0.2 ml ALG in normal saline or D/saline over 30 minutes. If no anaphylaxis, proceed to full dose. Dilute ALG to NOT LESS THAN 1 ml ALG in 10 ml and give over a minimum of 4 hours.
Cefotaxime	50 mg/kg IV pre-op and then bd (100 mg/kg/day)
Neoral Cyclosporin	150mg/m^2 PO pre-op and then bd
Methylprednisolone	600mg/m^2 IV pre-op
Azathioprine	60mg/m^2 PO pre-op then od post-op
Hydrocortisone	PRN 1 hour before ALG
Chlorpheniramine	PRN 1 hour before ALG

Live related transplant patients should have commenced azathioprine 4 days before operation date.

Prescribe:

Dopamine Infusion IV (renal dose) i.e. 2 mcg/kg/min.
0.45% Saline IV to replace urine losses
Morphine IV infusion (10-20 µg/kg/hour)

Oral Prednisolone starts on Day 1, 60mg/m^2/ d, for 5 days (see below)

POST OPERATIVE

DAY 1 On return from theatre

Let nurses sort out lines and commence fluids. Note that large urine output may already mean patient is relatively underfilled upon return to ward.

Urgent: **Plasma** U & E, PI creatinine, venous Astrup, FBC,
Urinary Na, K, Creatinine on return from theatre
CXR to check CVP line position

B. TRANSPLANT PROTOCOL B
FOR HIGHLY SENSITIZED PATIENTS WITH POSITIVE CROSS MATCH

Luckily these patients are rare. Immediately pre-operatively patients with a positive cross match will be immunoadsorbed on the Citem machine with a FACS cross match repeated every hour until the cross match is negative. The patient will then be taken off the machine and transferred to theatre within 1-2 hours. If for any reason the FACS cross match is still positive after 9 hours of immunoadsorption, the use of this kidney for this patient will be abandoned until a more suitable kidney becomes available.

In practical terms it takes 3 hours for the blood sample to get to Guy's Tissue Typing, the test to be performed and the result to be returned to the ward. It is therefore suggested that the first 6 samples, namely that taken pre immunoadsorption and those at 1,2,3,4 and 5 hours be sent in one batch and those taken at hourly intervals until the end of the Citem session be sent in a second batch. The results from the first batch, which will be available after 8 hours of immunoadsorption, should indicate that the apparent increased binding antibody titre is now falling such that one can predict that the 8-9 hour sample will be negative. This means in practice that we should be able to stop immunoadsorption on receipt of the first batch of results. This of course may have to be modified with further experience.

On Admission	As for Treatment Protocol A **except**
Premedication	Cyclosporin 480mg/m^2 orally Nifedipine 10 mg orally

To go to theatre with patient:

Cyclosporin	**150 mg/m^2 IV in 100 ml N/Saline**
Methylprednisolone	**600 mg/m^2 IV**
Frusemide	**250 mg IV**
Fresenius ATG	**6 mg/kg in 250 mls N/Saline**
Cyclophosphamide	**750 mg/m^2 IV**
MESNA	**150 mg/m^2 IV 4 hourly**

a) **Drugs**

ALG	(0.2 ml/kg/bd) further 3 doses given daily
NEORAL Cyclosporin	150 mg/m² bd p.o. at **10 am and 10 pm** (Intravenous dose 1/3 oral dose - if needed discuss with consultant/ registrar). Review dose according to blood levels (~200 µg/L). See Appendix 2 for further information.
Prednisolone	60 mg/m²/day in 2 doses daily for 5 days 30 mg/m²/day in 2 doses daily for days 6 - 30 30 mg/m²/day in 1 morning dose daily for 1 week 25 mg/m²/day in 1 morning dose daily for 1 week 20 mg/m²/day in 1 morning dose daily for 1 week 15 mg/m²/day in 1 morning dose daily for 1 week 10 mg/m²/day in 1 morning dose daily for 4 weeks then 10 mg/m² on alternate days
Azathioprine	60 mg/m²/day mane. Not to be given if Neutrophil < 1000 Restart when Neutrophil count > 1200. So write daily WBC differential on flow sheet
Cefotaxime	50 mg/kg bd IV until graft preservation fluid known to be sterile
Aspirin	37.5 mg x2 per week starting on day 2. Then Tues/Fri (18.75 mg x2 per week if weight < 15 kgs)
Nifedipine	5 - 20 mg PO bd
Nystatin	100,000 units (1ml) PO qds if still in nappies or having further ALG/ATG/OKT3 antibody treatment

Consider TB prophylaxis in foreign national patients

b) **Fluid Regime** 100% replacement of urine output with half normal (0.45%) Saline. Reduce to 75% replacement if output >500 mls/hour - discuss with Registrar. If plasma Na low, or urinary Na high (eg > 100 mmol/L) use alternate 500ml bags of 0.45% and 0.9% Saline for urinary replacement.

CVP to be kept around +4 to +8 with 4.5% Albumin or saline or blood if Hb low.

POST OPERATIVE

As Protocol A

a) **Drugs**

Cyclosporin 8 mg/kg orally bd
At 10.00 a.m and 10.00 p.m regardless of the 12 hour trough blood level unless it exceeds 600 ng/ml.

Prednisolone 60 mg/m² orally daily reducing to 10 mg at 1/12 and 5 mg by 2 months.

Cyclophosphamide 3 mg/kg orally daily at 18.00 and MESNA 50 mg orally at 18.00 hours, 22.00 hours and 06.00 hours after each dose of Cyclophosphamide for 3 months with careful monitoring of the total white count to maintain neutrophils >1000. After 2 to 3 months the Cyclophosphamide/MESNA to be replaced by Azathioprine 60 mg/m²/d, WBC permitting (discuss with consultant).

Fresenius ATG- 6 mg/kg over 6-10 hours IV in 250 mls Saline for 10 days unless it has to be discontinued because of drug reactions. The dose to be made up to the nearest 20 mgs and the rest of the vial retained. The next dose should be taken from this vial before using another one. Any opened ampoule can only be stored for 24 hours. It is important to remember that ATG is **VERY** expensive with Fresenius vials costing £150 each and if they are only used once with the residual thrown away then over £1,000 of drug may be lost in any one course of treatment. The first three treatments to be preceded (30 minutes) by Hydrocortisone 5mg/kg IV, Piriton 2.5 - 10 mg IV. Monitor WBC and lymphocyte count. If the WBC falls below 3,000 halve the dose of ATG - below 2,000 stop the ATG (N.B the Cyclophosphamide will have been stopped when the WBC falls below 4,000 i,e, before the reduction in the ATG. Tissue typing monitoring is important for this.

Cotrimoxazole 480 mg (1 tablet) daily orally for 6 months.

Acyclovir 200 mg bd orally.

b) **Fluid regime** as protocol A

c) **Investigations**

Daily haematological and biochemical investigations as for protocol 1, and **Cyclosporin levels which should be maintained between 200**

c) **Investigations**

Initially 4 hourly U & E, Ca, Phosphate, FBC for first 24 hours, urinary Na, K, Creatinine for 12 - 24 hours. Plasma creatinine should fall within 24 hours, otherwise primary nonfunction (ATN) is probably present.

PI creatinine twice daily for 10 days while an in-patient providing progress satisfactory.

Daily haematological, biochemical investigations and Cyclosporin levels.

1 day post op. Ultrasound and doppler or renogram scan of kidney.
Wean dopamine and morphine after 24 hours

Weekly MSU's, microscopy for candida.

d) **Other**

From day 1 actively mobilise the patient and make sure that they have their bowels open regularly. Begin educating the patient about drug regime from day 2.

e) **Tips**

Watch out out for hypocalcaemia in the early postoperative period (hours), particularly in children with a long history of dialysis, poor control of hyperparathyroifism.

Peripheral temperature gap + hypertension + low CVP on return to theatre usually means that patient is underfilled. Given 5 - 10 ml/kg 4.5% Albumin over 0.5 - 1 hour and monitor CVP changes. Repeat if necessary.

Watch respiratory rate and effort as it is easy to cause pulmonary oedema with fluid therapy, especially if patient oliguric. Remember in an emergency due to pulmonary oedema and no urine output, venesection of 5 ml/kg is curative usually.

Large requirement for fluid replacement (blood) with oliguria immediately postop - usually means bleeding from anastomosis.

Peripheral temperature gap + hypertension + high CVP on return to theatre usually means arterial vasoconstriction. Give hydralazine 0.25 to 0.5 µg/kg IV bolus, repeat if necessary. Oral Nifedipine 10 - 20 mg is also effective.

Hypertension + normal CVP + no temperature gap use frusemide if urine output present and hydralazine.
Sudden oliguria/ anuria - catheter blocked? Anastomotic bleed? urine leak?

INDICATION FOR RENAL BIOPSY

1 For patients with primary nonfunction of the kidney, i.e., an inability to reduce their serum creatinine spontaneously by day 3 to be biopsied on day 5 and every succeeding 7th day until good renal function is established.

2 All kidneys with evidence of "failing to thrive", i.e., although an initial fall in the plasma creatinine was achieved, it did not continue to fall lower than 150 -100 µmol/l.

3 All kidneys where there is a confirmed rise of greater than 10% over the previous days creatinine.

Pre-biopsy: All patients to have a haematological clotting screen, group and save and creatinine. The biopsy to be carried out under DDVAP cover (0.4 mcgm/kg IV over 10-60 minutes) if necessary.

Result of biopsy

a) **Resolving ATN** - re-biopsy in 5 days time after reconsideration of the use of any nephrotoxic drugs if renal dysfunction not resolved.

b) **Cyclosporin A toxicity** - only if Cyclosporin levels are high, consider reducing dose: check for any interacting drugs (see Appendix 2).

c) **Rejection** - this can be either cellular or vascular.

Cellular rejection - in first 6 weeks

Methyl Prednisolone 600 mg/m² in 10-20ml mls saline IV daily for 3 days **given slowly**. Then alternate day doses x 3 if baseline plasma creatinine not achieved - consider re-biopsy.

Vascular rejection -

1) If patient has NOT previously received any ATG give **Merieux ATG** (see Appendix 1 for dose and administration) or
2) If the patient has previously received Merieux ATG give **Merierux ALG** (see appendix 1 for dose and administration) or
3) If the patient has previously received Merieux ATG and ALG or they do not respond to either treatment, consider **repeat of Merieux dosage** or **OKT3** but only after discussion with the Consultant (see appendix 1 for dose and administration).

DRUGINTERACTION or CYA LEVEL EFFECT		
METRONIDZOLE	INCREASED - possible	
NICARDIPINE	INCREASED - rapidly	Expect to decrease dosage of Cyclosporin
NIFEDIPINE	DECREASED / or INCREASED	
PHENOBARBITONE	DECREASED	Expect to increase Cyclosporin dosage. Effect persists 7 days after stopping anticonvulsants.
PHENYTOIN	DECREASED	Expect to increase Cyclosporin dosage. Effect persists 7 days after stopping anticonvulsants.
RIFAMPICIN	DECREASED - markedly	Expect to have increase Cyclosporin dosage.
VERAPAMIL	INCREASED	For doses greater than 120mg/day may have to increase Cyclosporin dosage

Other drugs - see Sandoz Handbook on Cycylosporin A interactions

Out-Patient Clinic

The patients will be seen daily for six weeks, then 3x per week for 2 weeks, then twice per week for 2 weeks then weekly for 4 weeks and thereafter when clinically appropriate (ie 6 months out, once per month) assuming a smooth clinical course. No patient will be seen less than once a month during the first 12 months. Appropriate laboratory investigations will be carried out on each visit except for the blood sent to the Tissue Typing Laboratory at Guy's which will be 3 times per week in the first month, then at 3 months and again at 6 months.

The majority of patients will be discharged on triple therapy namely:-

NEORAL Cyclosporin A
Azathioprine or Cyclophosphamide
Prednisolone

NEORAL Cyclosporin A therapy will be monitored according to the blood levels. By one month they should be maintained at 150-200 ng.ml, from 1-6 months maintained around 150 ng/ml.

Prednisolone will be reduced as per protocol .

Azathioprine to be maintained at 60 mg/m²/day according to the WBC.

or

Cyclophosphamide to be maintained at 3 mg/kg/day daily for three months according to the WBC, at which time it will be changed to Azathioprine 60 mg/kg/day.

Cotrimoxazole to continue for 6 months post transplant, **only if patient received protocol B.**

All episodes of renal dysfunction (plasma creatinine > 10% above baseline) , once proven will be immediately admitted for renal biopsy.

Regular duplex or renogram and ultrasound scans after the day 1 scan to be performed **only** where clinically applicable.

At 6 months

For those patients who have had a relatively "easy immunological" time (i.e., no more than 2 rejection episodes) it is suggested that

over the next 6 months the NEORAL Cyclosporin A will be gradually reduced such that by one year the patient's Cyclosporin A levels are around 100-120 mg/ml.

For those patients who have had an "immunologically difficult" time (i.e, 3 or more rejection episodes or ATG, it is suggested as a guideline that the Cyclosporin A levels be reduced starting at 6 months and maintained at 150 ng/ml for one year.

Azathioprine will be maintained at 60 mg/m²/d depending on the WBC.

Cotrimoxazole - to be stopped at 6 months.

Birmingham

THE CHILDREN'S HOSPITAL RENAL UNIT

PAEDIATRIC RENAL TRANSPLANT PROTOCOL

Introduction

Although the services for end-stage management of children with renal failure are now largely based at The Children's Hospital, paediatric renal transplantation continues to be undertaken at The Queen Elizabeth Hospital. The lack of resident paediatric medical staff therefore necessitates close liason with the paediatric consultant staff, who are:

Dr M H Winterborn
Dr C M Taylor
Dr D V Milford

Middle-grade staff are also provide on-call cover, and all paediatric medical staff can be contacted via The Children's Hospital switchboard, the renal mobile phone (0831-096425) or at home (numbers displayed in West 3 office).

The current practice of confining renal transplantation to children over 15 kgs in weight will continue for the forseeable future.

It is important to bear in mind that as the children and their families have received all medical care at the paediatric center, they will feel insecure and anxious in a new setting, especially as they will not know the medical and nursing staff. Parents are accustomed to being fully informed of planned investigations, problems with their child's progress, changes in medication, and so on. It is therefore necessary to regularly communicate with the parents and children, and to build up a working relationship with them. This is especially important for practical procedures such as routine venepuncture, catheter changes, wound dressings, etc. Remember that it is natural for children to cry during painful procedures and that parents understand this - indeed, they are usually very useful allies at these times. Nonetheless, repetitive unsuccessful attempts alienate parents and children, so it is important to call for paediatric help at an early stage.

On admission

Clerk and examine the child; check weight, note average 24 hour urine output.
Take bloods for:

1. Na+, K+, urea, creatinine
2. Full blood count
3. Cross match 2 units of blood
4. 10 ml clotted blood for tissue typing cross match (if not already done)
5. Urgent microscopy of MSU, PD fluid

Note An ECG and routine CXR are not needed

Oral anti-hypertensives (in order of preference - **discuss with paediatrician)**

1. Nifedipine 2.5 - 10 mgs 4 hourly po
2. Labetalol 25 - 300 mgs qds po
3. Atenolol 25 - 100 mgs om po
4. Isosorbide dinitrate 5 - 20 mgs qds po
5. Minoxidil 1.25 - 5 mgs 4-6 hourly po
6. Enalapril 2.5 - 30 mgs om po (avoid using immediately post-transplant)

HYDRALAZINE 1mg/Kg/day. (Max 100mg/day)

Parenetral anti-hypertensives

1. Labetalol 0.5 - 3 mgs/kg/hour
2. Sodium nitroprusside 0.5 - 8 μgms/kg/min
   NB. 3 mgs/kg in 50 mls at 1 ml/hour = 1 μgm/kg/min

Inotropes

Dopamine 5 - 20 μgms/kg/min
NB. 30 mgs/kg in 50 mls at 1 ml/hour = 10 μgms/kg/min

Anticonvulsants

1. Diazepam 0.15 - 0.25 mg/kg iv **or** 5 mg rectally
2. Paraldehyde 0.1 ml/kg rectally
3. Clonazepam - use dose recommended in paediatric vade mecum

4. Sodium valproate 5 - 25 mgs/kg/dose bd po
5. Phenytoin 2.5 - 3.5 mgs/kg/dose bd po
6. Carbamazepine 5 - 12.5 mgs/kg/dose bd po

Fluids, CVP, BP

Intra-operatively:

A triple-lumen CV line is very valuable for intra- and post-operative care. **We would recommend either a Cook CV catheter (7 French, 15 cms length) or a Deltacath (7 French, 20 cms length).** The intra-operative CVP should be maintained at 5 - 8 cms H_2O using 5 mls/kg boluses of 4.5% HAS or equivalent; it is particularly important to ensure an adequate CVP prior to release of the clamps.

Post-operatively:

Fluids
1. 100% replacement of urine output with 0.45% saline
2. Insensible loss calculated as 15 mls/kg/day, given as 10% dextrose (increase replacement in febrile children)
3. CV line flush with 0.9% saline

NB 100% replacement of overnight urine losses should continue for the first 3 nights

THE CHILDREN'S HOSPITAL RENAL UNIT

PAEDIATRIC RENAL TRANSPLANT PROTOCOL

On admission

Clerk and examine the child; check weight, note average 24 hour urine output.

Take bloods for:

1. Na+, K+, urea, creatinine
2. Full blood count
3. Cross match 2 units of blood
4. 10 ml clotted blood for tissue typing cross match (if not already done)

Arrange urgent microscopy of MSU, PD fluid

Note An ECG and routine CXR are not needed

Obtain consent for transplantation.

Contact the duty paediatric nephrologist to discuss blood pressure, fluid status, bichemistry results, drug prescription and to advise on the estimated time of transplantation. As most children are on continuous cycle overnight peritoneal dialysis (CCPD), those admitted late in the day may need to commence dialysis soon after arrival on the ward.

Hyperkalaemia should be discussed with the paediatric nephrologist; treatments are:

K+ > 5.5 mmol/l Ca resonium 1 gm/kg rectally, or salbutamol 4 μgm/kg iv over 20 minutes (avoid in hypertension).
K+ > 6.0 mmol/l 1ml/kg of a solution of 50% dextrose and insulin (20 mls 50% dextrose + 10 units actrapid) and dialysis.

Drug prescription

Pre-operatively:

1. Acyclovir 10 mg/kg iv infused over 1 hour if **donor CMV +ve and recipient CMV -ve**
2. Methylprednisolone 10 mg/kg 1-2 hours pre-op, infused over 1 hour.

In theatre:

3. Azathioprine 2 mg/kg iv
4. Subcutaneous heparin 1000 units
5. Frusemide 4 mgs/kg iv prior to release of clamps, or mannitol 0.5 gm/kg

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Cover: Schematic diagram of the structure of a representative class I MHC molecule (HLA-A2). The α_1 and α_2 domains form a peptide-binding site with the binding groove, which faces the T-cell receptor at the top (see Chaps. 2 and 3). (This remarkable structure is described in detail by PJ Bjorkman et al., in *Nature* 329:506–512, 1987. Reprinted with permission.)

For Nava and our children, Itai, [illegible]
of my father, Joseph Israel Danov[illegible]
and books

Table 14-4
Sequential immunosuppressive protocol for pediatric kidney transplantation at UCLA

Pretransplant (6–12 hr)
Cyclosporine: 10 mg/kg orally if ATG or MALG is to be used;[a] 4 mg/kg orally if OKT3 is to be used, or if donor procurement history suggests an increased likelihood of ATN

Induction Therapy
1. ATG or MALG at 15 mg/kg/day or
   OKT3 1 mg for 2 days then 2.5 mg for body weight <30 kg and 5 mg for < 30 kg
   Continue until serum creatinine ≤ 2 mg/dl or 10 days
2. Azathioprine 1–2 mg/kg/day
3. Methylprednisone 10 mg/kg/IV intraoperatively and 1–3 hours prior to OKT3 dose for days 1–3; then prednisone 0.5 mg/kg/day (minimum dose-20 mg)
4. If OKT3 is to be used, give cyclosporine 6 mg/kg PO divided bid to reduce the formation of anti-OKT3 antibodies; dose increased when serum creatinine ≤ 2 mg/dl; cyclosporine unnecessary with ATG or MALG

Maintenance Therapy
1. Cyclosporine: 12 mg/kg/day divided bid or tid for children ≤6 years; give 500 mg/m²/day divided bid or tid[b]
2. Cyclosporine dosage is adjusted to achieve target levels (see Table 14-5) using the lower range if the child has not achieved a serum creatinine of less than 2 mg/dl by the 10 days that the anti-T-cell preparation must be concluded
3. Azathioprine: 1–2 mg/kg/day
4. Prednisone: Taper to approximately 0.15 mg/kg/day at 6 months

[a]ATG, MALG, and OKT3 are described in detail in Chapter 4.
[b]The cyclosporine and monoclonal or polyclonal antibody preparations should be overlapped for 1–3 days until therapeutic levels of cyclosporine are achieved.

Following sequential immunosuppression with polyclonal or monoclonal antibodies, most programs employ triple therapy for maintenance immunosuppression (see Chap. 4). The therapeutic target cyclosporine levels and prednisone and azathioprine doses are listed in Table 14-5. Table 14-6 summarizes the cyclosporine doses prescribed by the UCLA Pediatric Transplant Program to achieve target levels at different time intervals posttransplant in younger and older children.

Table 14-5
Therapeutic targets for sequential immunosuppressive regimen at UCLA Pediatric Transplant Program

Weeks After Transplantation	12-Hour Cyclosporine Whole Blood Trough Levels*		Prednisone Dosage (mg/kg)	Azathioprine Dosage (mg/kg)
	Polyclonal TDx (ng/ml)	HPLC (ng/ml)		
0–4	500–750	150–200	0.5 (minimum 20 kg)	2
4–8	350–500	125–175	0.33	2
8–12	300–450	100–150	0.25	2
12–16	250–350	80–125	0.18–0.20	2
16–26	200–300	75–100	0.13–0.18	2

*See Chapter 4 for discussion of cyclosporine monitoring techniques.

Table 14-6
Mean total daily cyclosporine dose* at UCLA in relation to patient age

Age (yr)	Months After Transplantation				
	1	3	6	12	24
2–12	16.6 ± 7.1	12.2 ± 7.3	10.6 ± 6.7	9.2 ± 6.6	6.2 ± 2.4
13–21	10.8 ± 4.2	7.5 ± 2.7	6.3 ± 2.5	6.0 ± 2.1	5.1 ± 2.0

*mg/kg body weight ± SD.

TRANSPLANT MANAGEMENT PROBLEMS IN CHILDREN

PERIOPERATIVE FLUID AND ELECTROLYTE MANAGEMENT

Preoperative Dialysis

Children, like adults, should be adequately dialyzed before transplantation. For the child on hemodialysis, a complete dialysis treatment should be performed within 24 hours of the surgery. If electrolyte values are within acceptable limits, it is often not necessary to dialyze immediately prior to transplantation. Chronic peritoneal dialysis patients rarely require additional dialysis before transplantation, although their peritoneal cavities should be emptied of fluid. When performing pretransplant dialysis of whatever type, aggressive fluid removal should be avoided in an attempt to minimize posttransplant delayed graft function. Similarly, the polyuric child should receive appropriate hydration prior to surgery.

Intraoperative Fluid Management

Precise intraoperative fluid management and maintenance of adequate vascular volume is essential to minimize posttransplant delayed graft function. Fluid management is particularly crucial when placing an adult kidney in a relatively small child. An adult donor kidney may sequester as much as 150 to 250 ml of blood, and to prevent hypotension this amount of fluid should be administered as isotonic crystalloid and colloid solutions before the renal vessels are unclamped. The central venous pressure (CVP) and arterial blood pressure should be closely monitored during surgery. The intraoperative CVP should be maintained at 10 to 14 cm H_2O, and the mean arterial pressure maintained above 70 mm Hg before vascular clamps are removed.

Aggressive fluid therapy may be insufficient to optimize the blood pressure, particularly in children whose myocardial function is suboptimal. If the mean arterial blood pressure is relatively low despite an adequate CVP, a low-dose dopamine infusion may elevate blood pressure and facilitate renal vasodilatation. Some programs routinely institute intravenous dopamine infusions at 2 to 4 mg/kg/min at the start of surgery. If mean arterial blood pressure (MAP) is inadequate to effect good renal perfusion (e.g., MAP < 60 mm Hg) to adult donor organs, the dopamine infusion rate can be raised to as high as 9 μg/kg/min with excellent results. Furosemide (2–4 mg/kg) and mannitol (0.5–1 g/kg) may be given during creation of the vascular anastomosis to facilitate urine output. When these drugs are administered, however, the urine output must be replaced to prevent hypovolemia.

Postoperative Fluid Management

The principles of posttransplant fluid management are discussed in Chapter 8. It is particularly important that small patients receiving relatively large kidneys maintain intravascular volumes and blood pressure. The CVP should be maintained in the range of 6 to 10 cm H_2O, and mean arterial blood pressure should remain above 70 mm Hg. Insensible fluid losses should be calculated and administered as 5% dextrose (either 400 ml/m^2 body surface or 40 ml/100 kcal metabolized). The urine output should be replaced "ml for ml" with 0.33% or 0.45% saline. Because urine volume can be prodigious after transplant, the dextrose is omitted from the urine replacement to avoid hyperglycemia. Supplemental fluid boluses (10 ml/kg of normal saline or 5% albumin solutions in saline) may be required to support blood pressure, reestablish an acceptable CVP, and restore urine output. Augmentation of fluid therapy and inotropic support may be required to keep mean arterial pressures at acceptable levels (e.g., ≥ 70 mm Hg). If the child is fluid overloaded, it may be appropriate to replace only a portion of the urine output for a few hours until the CVP is reestablished at a desired level.

Early initiation of dialysis may be appropriate for the child with delayed graft function, congestive heart failure, or electrolyte abnormalities. Either hemodialysis or peritoneal dialysis may be performed safely. It is important to avoid overly aggressive ultrafiltration and fluid removal since this can exacerbate acute tubular necrosis (ATN).

ACUTE TRANSPLANT DYSFUNCTION IN YOUNG CHILDREN

In children, as in adults, the principal causes of early acute allograft dysfunction are acute rejection, acute tubular necrosis, cyclosporine nephrotoxicity, prerenal azotemia, obstructive uropathy, urine leak, renal artery stenosis, and viral and bacterial infections. The differential diagnosis is discussed in detail in Chapter 8.

In children there may be subtle differences in the presentation of graft dysfunction. In small children who receive large kidneys, a small rise in the serum creatinine levels (e.g., 0.2–0.3 mg/dl) can reflect a significant diminution in allograft function. Since the muscle mass and creatinine production of a child is small, there may be no recognizable rise in the serum creatinine level despite graft dysfunction, and the most sensitive indicator of rejection in small chil-

dren is the development of hypertension. Even a modest elevation in serum creatinine, particularly in the context of a low-grade fever, should be presumed to be rejection until proved otherwise.

Because of the higher incidence of CMV seropositivity in adults, the use of kidneys from adult donors, although preferable because of enhanced graft outcome, results in a greater incidence of primary CMV infection in young children. The use of sequential induction immunosuppressive strategies also makes it more likely that severe CMV disease will appear. However, the aggressive anti-CMV prophylactic therapies now employed in many centers (see Chap. 10) may attenuate the typical disease course, and CMV infection may manifest as only modest fever and a minimal rise in the serum creatinine level. Urinary tract infections in young children may be clinically indistinguishable from acute rejection, and urine culture and urinalysis must not be omitted in cases of fever and graft dysfunction.

The diagnostic tools for the evaluation of graft dysfunction do not differ in children and adults. Ultrasound and radionuclide scanning are discussed in Chapter 11. Fine-needle aspiration biopsy and core biopsy are discussed in Chapter 12.

TREATMENT OF ACUTE REJECTION IN CHILDREN

Pulse Steroids

High-dose corticosteroid pulses are the mainstay of treatment of acute rejection in children, as they are in adults (see Chap. 4). Doses at different centers range from 5 to 10 mg/kg/day of methylprednisone intravenously for three to five days. Following pulse treatment, the maintenance corticosteroid dose is usually resumed at the prerejection level or recycled back down from the high levels that were used posttransplant. Some centers prefer oral prednisone pulses, in which case 3 to 5 mg/kg is given for three days followed by a tapering dose back to baseline levels over 2 to 3 days. It may be advisable to give furosemide (0.5–1.0 mg/kg) either orally or intravenously during high-dose steroid therapy to minimize fluid retention and hypertension.

OKT3 Monoclonal Antibodies

Approximately 20 to 30% of rejection episodes will not respond to high-dose steroids; OKT3 monoclonal antibodies will reverse up to 90% of such episodes. OKT3 is discussed in detail in Chapter 4 and the pediatric protocol for OKT3 administration is shown in Table 14-7. In children, as in adults, OKT3 can be administered on an outpatient basis after the first few doses. Before completion of the OKT3 course, the cyclosporine dose should be increased by 1 mg/kg/day over the pre-OKT3 level so that blood levels are somewhat higher than they were prior to treatment; this regimen reduces the incidence of rebound rejections. When rebound rejections do occur, they may be amenable to high-dose steroids.

It is wise to monitor the effectiveness of OKT3 by following the levels of CD3-positive T cells. Immunologic monitoring is mandatory during a second course of OKT3 since the development of OKT3 antibodies may abrogate the effectiveness of the drug. Children may regenerate the CD3/T-cell receptor complex more rapidly than adults, and twice daily dosing of OKT3 is occasionally necessary to effect successful rejection reversal. Following a first course of OKT3, up to 35% of children may develop anti-OKT3 antibodies. The titer of antibodies is usually low and can be overcome by increasing the OKT3 dose; however, approximately 15% of children develop high titers of antibody, which prevent further use.

The side effects of OKT3 are similar in children and adults. Children must be euvolemic prior to administration of the first

Table 14-7
Treatment protocol for children receiving OKT3*

Before initiating therapy
Chest x-ray to show no evidence of fluid overload
If weight is more than 3% above dry weight, start dialysis or vigorous diuresis to attain dry weight
Prior to first and second doses of OKT3
Acetaminophen 250 mg PO
Benadryl 0.5–1 mg/kg IV
Methylprednisolone 10 mg/kg IV 1–3 hours before OKT3
Dose of OKT3
Body weight <30 kg = 2.5 mg OKT3
Body weight >30 kg = 5 mg OKT3
Cyclosporine to be continued at half previous dose during course
Prednisone at maintenance dose levels after second dose of OKT3

*See also Chapter 4 and Table 4-6.

dose to prevent pulmonary edema. Fever is nearly universal, and diarrhea and vomiting occur in nearly half of all children treated. Severe headache is common and may represent a mild form of aseptic meningitis. There have been occasional fatalities associated with OKT3-mediated cerebral edema.

NONCOMPLIANCE

Psychosocial and emotional problems in children and adolescents undergoing dialysis and transplantation frequently manifest themselves as noncompliance with the therapeutic regimen. The importance of this problem cannot be overemphasized.

Frequency

At least 50% of pediatric cadaveric transplant recipients demonstrate significant noncompliance in the posttransplant period. This figure exceeds 60% in adolescents. Noncompliance is the principal cause of graft loss in 10 to 15% of all pediatric kidney transplant recipients; in pediatric recipients of retransplants this figure may exceed 25%. Reversible and irreversible episodes of graft dysfunction related to noncompliance occur in up to 40% of adolescents and are somewhat less frequent in younger children.

Prognostication and Recognition

It is difficult to prognosticate in the pretransplant period who will not comply posttransplant. A disorganized family structure, female sex, adolescence, and a history of previous graft loss due to noncompliance are all significant risk factors. Personality problems related to low self-esteem and poor social adjustment are found with higher frequency in noncompliant patients.

Noncompliance in children must be suspected when diminution in cushingoid features, sudden unexplained weight loss, or unexplained swings in the patient's kidney function or cyclosporine trough blood level are observed. After an acute rejection episode is reversed, psychological support is of the utmost importance if long-term graft function is to be salvaged.

Management

Prospective introduction of behavioral modification programs or other forms of psychological intervention have had moderate success in improving compliance. In the pretransplant period, an ongoing program of counseling should be undertaken in high-risk patients. Clearly defined therapeutic goals should be set while the patient is on dialysis, and family problems that are recognized in the pretransplant period should be addressed prior to activation on the transplant list. The presence of at least one highly motivated caretaker is a helpful factor in long-term graft success.

Adolescence brings with it rapid behavioral and bodily changes. The adolescent's strong desire to be normal conflicts with the continued reminder of chronic disease that the taking of medication engenders; this tendency is particularly true when medications are taken many times a day and alter the physical appearance. Ambivalence between the desire for parental protection and autonomy, combined with "magical" belief in his or her invulnerability sets the stage for experimentation with noncompliance. Adolescents with psychological or developmental problems may use impulsive noncompliance during self-destructive episodes. The transplant teams must be aware of these developmental issues so that they can initiate appropriate psychological intervention before the onset of significant noncompliant behavior.

GROWTH

Impaired statural growth frequently accompanies renal insufficiency in children and is improved little by dialysis. In general, the earlier in life ESRD occurs, the greater the lifelong growth retardation; when the onset of ESRD is in infancy, growth retardation is most severe. Potential etiologic factors for this growth failure include anorexia resulting from protein/calorie malnutrition, renal osteodystrophy, metabolic acidosis and other electrolyte disturbances, the accumulation of uremic toxins, anemia, and specific effects of the primary disease.

A successful kidney transplant can correct all of these problems. One of the most important aspects of kidney transplantation in children is the achievement of optimal posttransplant growth.

Estimation of Growth Impairment

Growth in children with chronic illness is best expressed by comparing their height to that of unaffected children. This comparison is made by using a so-called **standard deviation score** (SDS) for age, which expresses a patient's height in terms of standard deviations

APPENDIX 1
TRANSPLANT PROTOCOL FROM BRISTOL 1995
as referenced by Dr Mary O'Connor in Statement

GUIDELINES FOR MANAGEMENT OF CHILDREN (IE ALL PATIENTS FROM JOHN MILTON/ VICTOR NEALE) UNDERGOING RENAL TRANSPLANTATION

UK Transplant or the transplant co-ordinator will phone with the offer of a kidney. Often the Consultant Paediatrician is consulted directly. If the call comes to a junior medical member of staff then it is important to talk to Dr McGrav, Dr Chambers, Dr Tizard or the Senior Registrar immediately as usually only half an hour is available to accept the kidney.

ONCE KIDNEY IS ACCEPTED

Inform transplant co-ordinator if he/she has not already been informed.

Other individuals to be informed are as follows. The transplant co-ordinator may do this although it is important for the member of the junior medical staff to establish exactly who is to make which phone calls.

i Phone UK Transplant and arrange for kidney to be sent to Bristol if harvested from elsewhere.

ii Phone the patient and arrange for them to arrive as soon as possible.

iii Check with tissue typing if a recent serum is available for cross-matching. If there is a very recent specimen and the patient has not been transfused since, this specimen may be used for the direct cross-match which may then commence as soon as the kidney arrives. If a fresh sample is needed from the patient it is vital to take this immediately he/she arrives as the cross-match takes eight hours and delay postpones the operation.

iv Inform also:

a Ward and nursing staff

b Transplant surgeon

c Theatre and make provisional booking

d First on-call anaesthetist and ask him/her to contact Senior Registrar and/or Consultant on-call anaesthetist

ONCE PATIENT ARRIVES

1 Take blood samples before anything else. It is important that the 5 mls of clotted blood for tissue typing (and any other specimens the tissue typing laboratory require) are sent immediately on arrival of the patient.

In addition bloods need to be taken for full blood count, coagulation screen, renal SMAC (with U&E, creatinine, calcium and albumin to be available at the time of transplantation. Other results may be available later), serum for virology (baseline CMV titres) and cross-match 4 units of blood (2 packed cells 2 whole blood).

2.....

2 Complete paediatric check list pre-transplant. All aspects must be filled in. Note in particular the need to record target weight, blood pressure and normal urine output and body surface area. This check list must go with patient to theatre.

3 Set up intravenous infusion at maintenance fluids appropriate for size of patient and replacing any deficit on assessing difference between current and target weight.

4 Institute other investigations including chest X-ray, ECG, FBC, urea, urine culture.

5 If history of hyperkalaemia or potassium of greater than 5 mmol/l

a Fast cycle if on PD

b Give calcium resonium 1 gm/Kg PR if on haemodialysis and discuss with consultant if haemodialysis needed in view of chemistry

6 Talk to parents and obtain consent.

7 Write up immunosuppression to be given in the theatre. For all patients this will be Methylprednisolone 10 mg/kg i.v 5-10 minutes before vascular clamps are released.

8 Write up instructions for intra-operative blood transfusion on checklist once haemoglobin is known. This will be the number of pts of packed cells required to bring the patients haemoglobin up to 10 gms/dl.

9 Write up appropriate Mannitol dose on checklist (0.5 g/Kg 20% Mannitol ie 2.5 ml/Kg).

10. Write up induction dose of antibiotics iv augmentin 30 mg/kg (max 1.2g).

IN THEATRE

1. Insert CVP and arterial line.

2. Use normal saline, plasma or blood, (as appropriate) to raise CVP to - 8-10 cm H20 (6-8 mm Hg) before the vascular clamps are removed from the donor kidney. Aim to keep CVP at this level for the remainder of the operation. Please always take into account actual and target weights and overall hydration state.

3. Give intra-operative blood transfusion as per checklist instructions.

4. Give intra-operative immunosuppression as per checklist 10 minutes prior to the vascular anastimosis together with Mannitol see checklist for doses.

5. Start dopamine 2-3 ug/kg/min via central line

1.....

IMMEDIATE POST-OPERATIVE CARE

1 Allow nurses to make patient comfortable and connect up the monitoring equipment and lines, which will be as follows:

i Weigh bed

ii Rectal and toe temperature probes

iii Hewlett-Packard ECG, BP and CVP monitor or equivalent connected to CVP and arterial lines

iv Peripheral intravenous infusion(s)

v Urethral catheter

vi Ureteric catheter (in some cases only)

vii PD catheter spigotted and empty (if appropriate)

2 Write up the following drugs:

a Morphine 0.01-0.02 mg/kg/hour (half the patients weight in kg mg in 50 mls at 2 mls/hour) or

Papaveretum 0.02 to 0.04 mg/kg/hour or fentanyl as per selected protocol

b Methylprednisolone 10 mg/metre^2/day as b.d. dosage. First dose to be given 12 hours post-operatively

c Cyclosporin 6 mg/kg/24 hours written up as continuous infusion 3 mg/kg/12 hourly. This will be converted to Cyclosporin 15 mg/kg/day orally given as b.d. dosage when the patient is tolerating oral fluids

d Ranitidine 2 to 4 mg/kg/day orally (as bd dose)

e Dopamine 2 microgrammes/kg/minute - see drug infusion protocol

f Anti-thymocyte globulin (Fresenius) for those on high risk protocol only (ie previous graft or high cytotoxic antibodies) 4 mg/kg/day iv. Need to give test dose intravenously first.

g Other drugs such as Hydralazine or Frusemide may be written up when required

h Further antibiotic therapy is discretionary and would be used only if there was a history of recent infection in either the patient or the donor, or the recipient is known to have vesicoureteric reflux into their native kidneys. This should be discussed with the consultant.

i Acyclovir Post Renal Transplant

Check CMV status donor and recipient. If donor and recipient negative, no Acyclovir given. If donor positive [illegible] for 12 weeks regardless of recipient status. If donor negative and recipient positive, course given for six weeks.

Dosage • 800 mg po 2-6 hours pre op
• 800 mg po 24 hours post op
Thereafter according to GFR:

> 25 ml/m	6 hourly	• 800 mg po
10-25 ml/m	8 hourly	• 800 mg po
< 10 ml/m	daily	• 800 mg po
dialysis dependent	12 hourly	• 800 mg po

• half dose in under 2 years old

OBSERVATIONS:

Pulse, blood pressure, core and peripheral temperature, CVP and urine output should be measured hourly. One should aim to maintain:

i CVP between 8 and 12 cm H20 (6-9 mm Hg)

ii Temperature gap less than or equal to 2 degrees centigrade

iii Blood pressure to be decided on an individual basis within that patients normal target blood pressure guidelines

iv The patient should be weighed daily. It is important to note that weigh bed weights may differ markedly from pre-operative weights and that whilst changes in weigh bed weights are important no significance can be attached to the difference between weights made on different scales

v Optimal urine output to be decided on an individual basis. In polyuric patients this will be around 4 ml/Kg/hour initially falling to 2 ml/Kg/hour when stable. In previously anuric patients far lower urine outputs may be acceptable if A.T.N. has occurred Check transplant troubleshooter for management guidelines on response to failing urine outputs. Otherwise aim for at least 2ml/Kg/hour

FLUIDS

Arterial line 0.9% Heparinised saline at 3 mls/hour with a pressurised bag or 1-3 mls/hour heparinised 0.45% saline with a syringe pump. Take care not to confuse the 3 ml/hr flush device used with a pressurised bag with the 30 ml/hr device used with a syringe pump.

Central line half normal saline/2.5% dextrose plus or minus KCL at rate to replace all losses (sodium and potassium content to be adjusted according to urine electrolytes)

Peripheral line at insensible loss and containing drug infusions

5.....

INVESTIGATIONS

U & E (urine and plasma, glucose and calcium) (6 hourly for 24 hours, [illegible] hourly for next 24 hours and thereafter 24 hourly)

Full blood count, renal SMAC daily and chest X-ray daily for first [illegible] three days

Urine cytology daily

Cyclosporin levels, urine culture, magnesium, 24 hour urine, creatinine clearance protein clearance twice weekly. Urine and saliva for CMV once weekly

A doppler ultrasound renal scan should be performed daily if there are doubts about initial function and thereafter if there are [illegible] deterioration in renal function. The decision for a scan should be taken by the Paediatric Consultant and timing discussed with Dr Howarth.

Comments/corrections in writing to

Dr ME McGraw - Consultant Paediatrician and Nephrologist
or
DR D E Holland - Consultant Anaesthetist/Intensive Care

Updated January 1995 [illegible]

BRISTOL ADULT

SOUTHMEAD HOSPITAL KIDNEY TRANSPLANT PROTOCOL

1. Recipient Selection

- Physician to select recipient and liaise with surgeon

Co-Ordinator will notify the patient
" " informs ward
" " books theatre/anaesthetist
" " informs tissue-typing
Physician/Surgeon to decide whether ITU post op care is needed

2. Recipient preparation

- Nil by mouth (remind patient on phone)
- May need dialysis (liaise with unit)
- Weight
- Residual daily urine volume
- Peripheral pulses recorded in patients > 50
- ECG and CXR
- Elecs, creat, glucose, ferritin
- FBC, INR, APTT - if on anticoagulation
- Group and save for patients with haemoglobin > 9
- Cross match 2 units whole blood if Hb > 7 g/dl, < 9. 4 units if Hb < 7.
- Serum for CMV Ab
- Serum to tissue-typing for LCTA
- MSU,
- Shower
- Consent, Pre-med
- Anti-embolism stockings
- Check most recent cytotoxic antibody status on computer. If >35% (unseparated) patient needs Aza: if >70% needs ATG.
- **The SHO must record in patients notes and on the renal computer system the donor and recipient HLA types, and in the notes the result of cross match and the donor CMV status.**
- Check Tx data screen - any fertile female who is Rhesus negative receiving a rhesus positive kidney must have 500 u of ANTI D

3. Cyclosporin (Cya)

- **Pre-Op:** 15 mg/kg orally to be given 4 hrs or more pre-operatively if possible. If less than 4 hrs before anaesthetic loading dose should be 3 mgs/kg i.v. should be given
- **Post-Op:** 1st dose to be given on the evening after surgery
- 2 mg/kg/12 hr i.v. till able to absorb from stomach
- Then 6 mg/kg/12 hourly orally. The first post-operative dose should be given dependent upon return from theatre. Those patients undergoing transplantation in the evening will receive their first post-operative dose on the morning round. Those undergoing morning transplantation will receive their first dose on the evening round.
- **DOSAGE SHOULD BE DOUBLED IN PATIENTS ON KNOWN ENZYME INDUCERS E.G. PHENYTOIN, CARBEMAZEPINE, PHENOBARBITONE.**
- Check blood levels daily from days 1-9 and then Mon, Weds, Frid.
- Send samples pre dose to reach lab by 9.30

3. Cyclosporin (cont)

- In patients without immediate post-op diuresis:
  (urine output < 30 ml/hr)
  reduce CyA to 4.0 mg/kg/12 hourly orally (1.0 mg/kg/12 hourly i.v.)
  add Azathioprine 2.5 mg/kg/day (same dose oral or i.v.)
- When transplant function picks up Cyclosporin should be increased to full levels and Azathioprine withdrawn over one week. The Cyclosporin levels should be measured throughout the first week, but no action taken on these results until 7 days have passed. For the period from the end of the first week until 4 weeks the serum Cyclosporin levels should be not less than 250 mg.

4. Steroids (Pre and Post-op)

Starting dose of oral Prednisolone to be administered on pre-op basis and is dependent upon patient weight.

Patients less than 50 kgs	-	starting dose	15 mgs of Prednisolone daily
Patients weighing 51-70 kgs	-	" "	20 mgs of Prednisolone daily
Patients weighing 71-80 kgs	-	" "	25 mgs of Prednisolone daily
Patients weighing > 80 kgs	-	" "	30 mgs of Prednisolone daily

Patients should remain on their starting oral dose for three weeks initially. Providing there has been no rejection episode steroids should be reduced at a rate of 2.5 mgs per fortnight until reaching a baseline of 5 mgs daily for those patients weighing less than 55 kgs and 7.5 mgs daily for those weighing more than 55 kgs.

Patients who have undergone a major rejection episode should continue on the higher dose of Prednisolone until three weeks after the final administered dose of antirejection therapy and continue to be tailed off down the same scale as the non-rejectors.

Patients who are unable to receive oral steroid medication should receive Prednisolone in the same dose intravenously.

Further modification may be made following discussion at the Renal Transplant meeting.

5. Azathioprine (Aza)

- Not routine treatment
- Add to reduced CyA dose in case of primary non-function
- Add low dose Aza (1 mg/kg/day) for repeated rejection (see below)
- Add low dose Aza (1 mg/kg/day) to standard CyA protocol for recipients with current/most recent cytotoxic antibodies > 35%.
- Avoid concurrent Allopurinol: if patient on Allopurinol discuss.

6. Anti-thymocyte Globulin (ATG) Merrieux - Thymoglobulin - rabbit

An equine ATG is also available from Merrieux - Lymophoglobuline - which should not be used unless patients have been previously exposed to the rabbit antigen. The doses of the equine variety are four times as high, although they come in equal volumes. It is essential to specify on prescription that rabbit ATG is wanted

- Not routine treatment
- Reserve prophylactic ATG for recipients with cytotoxic antibodies > 75% or 2nd transplants when the first graft was lost with early rejection
- Rescue therapy for steroid resistant rejection (see below)
- Dose: Start with 2 mg/kg/day for 7-10 days. Normal dose stays between 1.25 and 2.5 mgs/kg/day.
- Administer via central line if possible or in large peripheral vein
- Prior to first dose administration give Chlorpheniramine 10 mg i.v. and hydrocortisone 100 mg i.v. First dose of ATG diluted to 500 mls, Rate of administration - first hour 30 ml and then give at 75 ml/hr Subsequent doses, given centrally if possible, dilute in 250 mls and given at 50 ml/hr; if peripheral, use a large forearm vein, dilute to 500 ml and give at 50 ml/hr
- Monitor total lymphocyte count to ensure adequate response - aim for a count of $<0.2 \times 10^9/l$. Enter counts on to immunosuppression screen.

7. Anti-rejection therapy

- Methyl prednisolone 500 mg/day i.v. for three days
- Repeat pulse steroids if further rejection > 4 days after last pulse dose
- ATG rescue therapy to be reserved for the following circumstances:
  - No response to pulse steroids
  - Further rejection within 4 days of last pulse **(NB confirm with biopsy)**
  - To treat the 3rd rejection crisis within the first three weeks
- Dose: 2.5 mgs/kg/day
- Reduce CyA dose by a third during ATG, and return to full dose 2 days before completion of ATG
- Start Aza 1 mg/kg/day 5 days before the end of ATG course
- Give prophylactic nystatin during heavy immunosuppression
- Give prophylactic Acyclovir during heavy immunosuppresion (see below)

8. Antibiotics

- Augmentin 1.2 g on induction (single dose)

9. Ranitidine - 150 mg b.d. (full dose)

- Full dose to start pre-op in those with previous proven peptic ulcer
- Full dose during anti-rejection therapy
- Half dose if oliguric
- To continue until steroid dosage reduced to baseline maintenance

10. Acyclovir

- Prophylaxis against CMV if either donor or recipient CMV antibody positive
- Dosage: 800 mg orally 2-6 hrs pre-op
  800 mg orally as soon as bowel sounds

Thereafter according to estimated GFR:-

GFR < 10 ml/min	:	800 mg daily
GFR 10-25 ml/min	:	800 mg 8 hourly
GFR > 25 ml/min	:	800 mg 6 hourly
Haemodialysis dependent	:	800 mg 12 hourly
CAPD dependent	:	800 mg 48 hourly

- Assume GFR > 25 ml/min if early diuresis > 100 ml/hr
- Continue for 12 weeks

11. Peri-op fluid management

- The anaesthetist should insert a CVP line on induction. Aim for CVP of 5-10 cms H_2O prior to surgery
- CVP monitoring routine in all patients. Commence CVP monitoring immediately post-operatively. Attach CVP line to distal lumen and catheter. Continue CVP monitoring whilst awaiting CXR to confirm position of line on ward.
- Give blood to replace significant blood losses
- Check Hb if CVP stays low with clear fluids
- CVP measured with patient supine (max. 1 pillow)
- Measure CVP with zero to be marked on patient's chest wall (mid axillary line)
- Give 100 ml boluses of 4.5% HAS or Gelofusine over 5 minutes if CVP < 6.5 cm water
- Recheck CVP immediately after bolus and repeat bolus infusions to achieve target CVP
- Do not wait for next hour to check CVP after bolus
- Give bolus of colloid to a maximum of 1.0 litre: then inform SHO who must examine the patient
- Aim to keep CVP in range 6.5 - 10.5 cm water (5-8 mm Hg)
- Replace urine output + 30 ml hourly with rotating litre bags of 0.9% saline to two of 5% dextrose
- Consider adding potassium to infusion if diuresis > 250 ml/hr (check serum potassium first)

12. Post-op hypertension

- Ensure adequate analgesia
- If BP > 200/110 give 5-10 mgs Nifedipine capsules buccally and repeat as necessary

13. Monitoring progress

- Daily weight
- Daily serum creatinine and elecs, daily 24 hr.urine for creatinine, urea, protein
- Daily FBC
- Daily CSU or MSU - SHO to see MSU results
- CyA level daily days 2-9, then Mon, Wed, Fri
- Ca, PO4, LFT's, Protein, Albumin twice weekly
- Doppler ultrasound of graft 24-48 hours post-op and one at discharge
- Repeat US for clinical problems (creatinine rising, no function, graft swollen, leak suspected etc)
- Standard frequency of follow-up:-

Weeks	1 & 2		Daily
Weeks	3 & 4		Tues (clinic): Fri (clinic)
Weeks	5 & 6		Tues (clinic):
Weeks	6 - 8		Fortnightly
Weeks	8 - 12		Fortnightly
Months	3 - 6		Monthly
After	6 - 12	mths	Two monthly
>	1	year	Three monthly
>	3	years	Four monthly

14. Drains and Catheters

- Wound drainings to be removed when drainage < 30 ml/24 hr
- Urinary catheter - day 6
- Infant feeding tube - day 5 (or falls out) - this must be discussed with transplant surgeon

PAL/CT/TGF/BJ
31 01 95 (amended)

Standards and Guidelines Committee

Policy for the administration of intravenous fluids to children aged from 1 month until the 16th birthday: reducing the risk of hyponatraemia.

Summary	This policy outlines the BHSCT approach for administration of intravenous fluids to children aged from 1 month until the 16th birthday with particular reference to reducing the risk of hyponatraemia. It maps the advice issued in March 2007 from the National Patient Safety Agency (NPSA) and September 2007 from the Northern Ireland Regional Paediatric Fluid Therapy Working Group on how to reduce the risks associated with administering intravenous infusions to children. This is fundamentally a document aimed at prevention of hyponatraemia and not treatment.
Purpose	To improve the safe use of intravenous fluid in children and reduce the risk of hyponatraemia.
Operational date	March 2008
Review date	March 2010
Version Number	V4
Supersedes previous	V3
Director Responsible	Medical Director
Lead Author	Dr. Peter Crean
Lead Author, Position	Consultant Paediatric Anaesthetist, RBHSC.
Additional Author(s)	Dr H Steen, Associate Medical Director.
Department / Service Group	Social Services, Family and Child Care
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Reference Number	
Supercedes	N/A

Date	Version	Author	Comments
25 August 2009	V 3.1	JR Johnston	Draft version 3
14 September 2009	V 3.2	JR Johnston	Minor RMcL amendments
16 September 2009	V 3.3	JR Johnston	8.3.4; Appendix 6 changes Final Draft for RQIA
17 September 2009	V 3.4	JR Johnston	4.1; 8.4 - DKA Fluid chart change
17 September 2009	V 3.5	JR Johnston	Appendix 4 changes
February 2010	V 3.6	JR Johnston	Trigger list

Policy Record

		Date	Version
Author (s)	Approval	27/03/2008	1.2
Director Responsible - Dr A Stevens	Approval	27/03/2008	1.2

Approval Process – Trust Policies

Policy Committee	Approval		
Executive Team	Authorise		
Chief Executive	Sign Off		

Approval Process – Clinical Standards and Guidelines

Standards and Guidelines Committee	Approval		1.2
Policy Committee	Approval		
Executive Team	Authorise		
Appropriate Director	Sign Off		

Summary

Reference No: SG001/08

Title:
Policy for the administration of intravenous fluids to children aged from 1 month until the 16th birthday: reducing the risk of hyponatraemia.

Purpose:
To improve the safe use of intravenous fluid in children and reduce the risk of hyponatraemia.

Objectives:
This Policy sets out recommended practice for everyone who looks after children receiving intravenous fluids. It is based on regional and national guidance, ongoing clinical audit, published literature and is also aimed at specifically reducing the risk of hyponatraemia.

It should be considered alongside the guidance from the National Patient Safety Agency Patient Safety Alert 22[1], and the Regional Paediatric Fluid Therapy Group wallchart[2].

Policy Statement(s):
1. The Paediatric Parenteral Fluid Therapy wallchart[2] forms the basis of BHSCT guidance on fluid prescription in paediatric patients aged from 1 month until the 16th birthday.
2. Sodium chloride 0.18% with glucose 4% will be withdrawn from general use in all BHSCT ward areas that treat children and the availability of these fluids will be restricted to critical care areas and other specialist wards such as renal, liver and cardiac units.
3. This policy and wallchart will be disseminated throughout the BHSCT.
4. Information about the availability of infusion fluids throughput the BHSCT will be attached to the Paediatric Fluid Guideline wall chart[2].
5. A new fluid prescription/ balance chart will be developed for the prescription of fluids for all children treated in the BHSCT.
6. All staff involved in prescribing, administering and monitoring IV fluids to such children will be made aware of this policy and the Paediatric Parenteral Fluid Therapy wallchart[2] through the BHSCT intranet and Service Group dissemination.
7. The BHSCT will implement the following governance measures – incident reporting using a set of reporting 'triggers' and formal auditing.

Chief Executive/ Director *(delete as appropriate)*	**Author**
Date:	**Date:**

Contents Page:

Full Description

Reference No: SG001/08

1. ***Policy for the administration of intravenous fluids to children aged from 1 month until the 16th birthday: reducing the risk of hyponatraemia.***

2. **Introduction:**

The development of fluid-induced hyponatraemia in the previously well child undergoing elective surgery or with mild illness may not be well recognised by clinicians.[1]

Since 2000, there have been four child deaths following neurological injury from hospital-acquired hyponatraemia reported in the UK.[1] International literature cites more than 50 cases of serious injury or child death from the same cause, and associated with the administration of hypotonic infusions.[1]

In March 2007 the National Patient Safety Agency (NPSA), with Alert 22, issued advice on how to reduce the risks associated with administering infusions to children[1].

In April 2007, with DHSSPSNI circulars[3,4], NHS organisations in Northern Ireland were tasked to produce and disseminate local clinical guidelines for the fluid management of paediatric patients based on the suggested NPSA guidelines template. The Northern Ireland Regional Paediatric Fluid Therapy Working Group produced an intravenous fluid clinical guideline in accordance with NPSA guidance[1]. This was disseminated to each HSC Trust for local implementation and monitoring.

In February 2009 the Regulation and Quality Improvement Authority (RQIA) published an independent review *"Reducing the risk of hyponatraemia when administering intravenous infusions to children"* which dealt with the implementation of recommended actions outlined within the NPSA Alert 22 and dissemination of the clinical guidelines / wall chart throughout HSC Trusts and independent hospitals. (see appendix 7.)

This document, using both the NPSA guidance and the RQIA recommendations, outlines the BHSCT policy for administration of intravenous fluids to children aged from 1 month until the 16th birthday with particular reference to reducing the risk of hyponatraemia; it is fundamentally a document aimed at prevention of hyponatraemia and not treatment.

3. **Purpose:**

To improve the safe use of intravenous fluid in children and reduce the risk of hyponatraemia.

4. **The scope:**

4.1 Applicable to all children more than 1 month and until their 16th birthday throughout the Belfast Health and Social Services Trust (BHSCT).

It is relevant for all general inpatient areas that treat patients from this age range (even if it is only occasionally) and includes the post-operative scenario, emergency departments, day case departments and the ambulance service.

This policy (and attendant fluid prescription chart) is not intended to apply to paediatric

and neonatal intensive care units, specialist areas such as renal, liver and cardiac units where it is used to replace ongoing losses of hypotonic fluids, or those suffering from burns or diabetic keto-acidosis (DKA) where hypotonic solutions may have specialist indications.

Children receiving long term Total Parenteral Nutrition (TPN) are not covered by the conditions of this policy.

4.2 Young people

As a child progresses through the teenage years there is a transitional stage of physical development i.e. adolescence, as that child progresses through towards adulthood. They will be referred to as 'young people' and many are cared for in adult wards by staff who generally treat adults.

The DHSSPSNI indicates that this paediatric fluid therapy guidance relates to all children from 1 month until their 16th birthday, regardless of the ward setting, except in the ICU and specialist areas mentioned above.

5. Objectives:

This policy sets out recommended practice for everyone who looks after children receiving intravenous fluids. It is based on regional and national guidance, ongoing clinical audit, the published literature and is also aimed at specifically reducing the risk of hyponatraemia.

It should be considered alongside the guidance from the National Patient Safety Agency Patient Safety Alert 22[1], and the Regional Paediatric Fluid Therapy Group wallchart[2] and the RQIA recommendations[5].

6. Roles and Responsibilities:

All professionals caring for children must:-

- be familiar with the signs of hyponatraemia.
- be familiar with its emergency management.
- ensure that they have received adequate training in intravenous fluids appropriate to their role.
- if they exclusively care for young people in an adult ward, know where to obtain expert paediatric should it be needed. (Appendix 5).
- be familiar with the guidance on intravenous fluids for children outlined by the Regional Paediatric Fluid Therapy Group wallchart[2].

7. The definition and background of the policy:

A child, for the purposes of this policy, is defined as being aged from 1 month up to their 16th birthday.

Hyponatraemia is an abnormally low concentration of sodium (Na) in serum. The normal range is generally agreed to be 135 – 145 mmol/L.

Hyponatraemia is defined as a plasma Na of less than 135 mmol/L. It represents an excess of water in relation to sodium in extracellular fluid and is described as severe or significant if below 130 mmol/L.

Significant acute hyponatraemia is defined as a decrease in plasma sodium from normal to less than 130 mmol/L in less than 48 hours.

Symptoms are likely with serum Na <125 mmol/L or if the serum Na has fallen rapidly; greater than 5 mmol/L decline in 24 hours.

The main causes of hyponatraemia in children are:

- Administration of hypotonic fluids, intravenous or enteral (e.g. excessively dilute formula or sodium chloride 0.18% and glucose 4% (No 18 solution))
- Conditions with impaired free water excretion and high anti-diuretic hormone levels
  - Meningitis, encephalitis, pneumonia, bronchiolitis, sepsis
  - Surgery, pain, nausea and vomiting
- Gastrointestinal fluid losses

Less common but important causes are:

- Adrenal insufficiency (Congenital Adrenal Hyperplasia, Addison's Disease)
- Defect in renal tubular absorption, including obstructive uropathy
- Psychogenic polydipsia

The main symptoms of hyponatraemia relate to its central nervous system effects; cerebral oedema, seizures and death. Warning signs may be non-specific and include nausea, malaise and headache.

All children are potentially at risk, even those not considered to be obviously 'sick'. The complications of hyponatraemia often occur because of the inappropriate management of intravenous fluids but they can also occur with inappropriately managed oral fluid regimes. Vigilance is required for all children receiving fluids.

Children particularly at risk are those who are postoperative, have gastrointestinal fluid losses or who have bronchiolitis, CNS injuries or burns. These risk factors also apply to young people.

8. Policy / Guideline description:

The NPSA recommended in Alert 22 the following actions:-

1. **Remove 'No. 18 solution'** from general areas that treat children and restrict availability to specialist areas except in critical care and specialist wards such as renal, liver and cardiac units.
2. Produce and disseminate **clinical guidelines** for the fluid management of paediatric patients.
3. Provide adequate **training** and supervision for all staff involved in the prescribing, administering and monitoring of intravenous infusions for children.
4. Review and improve the design of existing intravenous fluid prescriptions and **fluid balance charts** for children.
5. Promote reporting of hospital acquired hyponatraemia **incidents** via local risk management reporting systems. Implement an **audit** programme to ensure adherence to the above.

The 16 RQIA recommendations (appendix 7) map to the above NPSA recommendations:-

NPSA	RQIA
1	1, 2
2	3, (4), 5, 7
3	6, 7, 8, 9, 10
4	11
5	12, 13, 14,
6	15, 16

The specific actions that the BHSCT will institute in order to limit the production of hospital acquired hyponatraemia are detailed below and are mapped to the RQIA recommendations.

8.1.1 *Remove 'No. 18 Solution'*
NPSA 1 RQIA 1
Sodium chloride 0.18% with glucose 4% has been withdrawn from general use in all BHSCT ward areas that treat children and the availability of these fluids is restricted to critical care areas and other specialist wards such as renal, liver and cardiac units. A table showing areas permitted to stock or order 'No.18 solution' is given in Appendix 6.

8.1.2 *NPSA 1 RQIA 2* Any area that is still permitted to stock 'No. 18 solution will arrange for the provision of additional labelling or separate storage.

8.1.3 *NPSA 2 RQIA 6* Information about the availability of infusion fluids throughput the BHSCT (Appendix 4) will be attached to the Paediatric Fluid Guideline wall chart[2].

8.1.4 The BHSCT's list of sanctioned standard maintenance fluids is given in Appendix 4.

Where a senior clinician(s) considers that a "special" maintenance infusion fluid is required, then this alternative choice for fluid maintenance must be endorsed by the Chief Executive of the Trust with clear documentation of the reasons for that endorsement.

8.2 *Clinical Guideline*
NPSA 2 RQIA 3,5,7
The Paediatric Parenteral Fluid Therapy wallchart[2] forms the basis of BHSCT guidance on fluid prescription in paediatric patients within the previously defined age range. This policy and wall chart will be disseminated and displayed throughout the BHSCT; to all wards that accommodate children aged from one month until their 16th Birthday including Emergency Departments, Adult Wards, Theatre and Intensive Care Units.

This will replace any previous wallchart including the 2002 wallchart issued by CMO entitled "Any Child Receiving Prescribed Fluids is at Risk of Hyponatraemia". All previous versions of the chart should be removed.

8.2.1 *NPSA 2 RQIA 7* The BHSCT will develop policy and guidelines on the general principles of intravenous therapy for adults and children.

Until then, this policy will form the basis of guidance on fluid therapy in children within the BHSCT and, as for all BHSCT policies, it will be reviewed and implemented throughout the organisation.

8.2.3 *NPSA 2 RQIA 3* All medical and nursing staff should base their intravenous fluid practice for children, young people (and indeed adults) on the following best practice model of:-

- administer appropriate therapy for shock such as fluid boluses
- measure/estimate and correct any fluid deficit
- prescribe a fluid maintenance fluid regime.

Treatment of these elements of the overall fluid status is outlined in the Paediatric Parenteral Fluid Therapy wallchart[2].

The fundamental layout selected for this guideline complements a structured approach to patient clinical assessment. A sequence of questions is offered that prompts the clinician to

- assess for the presence of shock and guides treatment, if required;
- further assessment of whether there is also a deficit to be considered and then
- calculation and prescribing for maintenance requirements is also included.

8.2.4 This policy, centred on children, has many features that indicate good practice for young people and adults. An intravenous fluid therapy practice based on using

- an individual patient's weight in kilograms
- fluid administration based on a millilitres/hour prescription

is commended rather than blanket prescriptions based only on fluid volume.

8.2.5 Baseline Assessment

Good practice guidelines on monitoring body weight, electrolytes/urea and fluid balance should be followed. Again, these recommendations apply to adults as well as children.

An essential preliminary to these assessments is to accurately measure the body weight in kilograms or failing this, to make an estimate. This must be cross-referenced with the child's age to minimize the risk of error.

In the emergency situation an estimation of the child's weight should be made and an accurate weight obtained as soon as practically possible.

Baseline measurement of electrolytes and urea should be made unless the child is healthy and scheduled for elective surgery when it may be considered unnecessary.

8.2.6 Shock therapy

Shocked or collapsed children must immediately receive fluid boluses as outlined on the Regional Paediatric Fluid Therapy Group wallchart[2].

Good practice would indicate that the response to fluid therapy is closely observed and if there is no response by the time 40 mls/kg has been administered, senior medical advice and help is required.

Note that special treatment is needed for children with diabetic coma and trauma and the need to obtain senior advice and help is highlighted.

8.2.7 Fluid Deficit management

Calculation of the overall fluid deficit and the prescription of deficit replacement should only be undertaken by a doctor experienced in caring for dehydrated patients. The recommended fluid is sodium chloride 0.9% and it must be prescribed separately. The rate at which it is given is determined by the degree of dehydration and a relevant electrolyte sample.

For those caring for young people in a general adult ward, and who may not have such experience, they should ensure that they can avail themselves of advice from the sources as detailed in Appendix 5.

8.2.8 For advice regarding the estimation of the percentage of dehydration which is required for the fluid deficit calculation, the table in Appendix 2 should be consulted.

8.2.9 Maintenance fluid therapy
When prescribing maintenance fluids to children, young people and adults, the following scheme would be standard practice. For

- children use the calculations as indicated in the Regional Paediatric Fluid Therapy Group wallchart[2].
- young people and adults prescribe
    - 2 litres fluid for females over the weight of 40 kg.
    - 2.5 litres fluid for males over the weight of 60 kg.

8.2.10 The type of fluid selected must be tailored to the patient's needs as set out in the guideline. For example, following surgery, children who require intravenous fluids will be prescribed either sodium chloride 0.9% with or without pre-added glucose or Hartmann's solution in the post-operative period for maintenance fluid needs.

8.2.11 Children must not receive intravenous fluids unnecessarily. This guideline emphasises that assessment of each patient should include a decision on whether oral fluid therapy could be appropriately initiated instead of intravenous therapy and further prompts reconsideration of this question when IV therapy is reviewed.

8.2.12 This advice does not override or replace the individual responsibility of health professionals to make appropriate decisions in the circumstances of their individual patients, in consultation with the patient and/or guardian or carer or for consultation with a more senior clinician. This would, for example, include situations where individual patients have other conditions or complications that need to be taken into account in determining whether the guidance as detailed in the wallchart[4] is fully appropriate in their case.

8.3 Training
NPSA 3 RQIA 3,6,8,10
The BHSCT will use various forms of training on paediatric fluid management; didactic lectures, staff induction training and computer based training:-

1. a training presentation in the policies and guidelines section of the Intranet. This multidisciplinary presentation is accessible from any computer terminal within the BHSCT.
2. BMJ e-learning module
3. 'Training Tracker' (Multimedia Design Studio Limited).

The BHSCT advocates the adoption of a regional computer based educational tool that allows:-

- creation of an unlimited number of educational and training courses; to include mandatory modules.
- 'training' of all grades of staff.
- content of the training to be tailored to our own needs.
- tracking
    - who has taken each module.
    - who has not taken each module.
    - who has passed and who has failed.
    - precisely which questions each trainee got right and wrong.
- competency assessment tools.
- training record to be obtained at any time.
- to award personalised certificates to those who reach a stated passmark.

8.3.1 *NPSA 3 RQIA 6,8,10* All staff involved in prescribing, administering and monitoring IV fluids to children will be made aware of this policy and the Paediatric Parenteral Fluid Therapy wallchart[2] through the BHSCT intranet and Service Group dissemination.

All staff working exclusively with children and especially those prescribing fluids to children will be encouraged to ensure they are conversant with the knowledge required to prescribe intravenous fluids to children and that it is within their scope of practice.

They will be encouraged to use the intranet training presentation and the BMJ learning module on hyponatraemia - http://learning.bmj.com/learning/search-result.html?moduleId=5003358

The production of the certificate on completion of the above module may be sought at staff assessments, RITAs, performance review, personal development plans and appraisals.

The future BHSCT policy and guideline on the general principles of intravenous therapy (8.2.1) will also be available in the various training modules.

8.3.2 *NPSA 3 RQIA 6,8* All professionals caring for children must be familiar with the signs of hyponatraemia and its emergency management.

8.3.3 *NPSA 3 RQIA 6,8* For those caring for young people, they should either have received adequate training in intravenous fluids or if they exclusively care for young people in an adult ward, they should know where to obtain such expertise on children should it be needed. (Appendix 5).

Furthermore, they should be familiar with the guidance on intravenous fluids for children outlined in this policy and Regional Paediatric Fluid Therapy Group wallchart[2].

8.3.4 *NPSA 3 RQIA 9* The BHSCT has identified that young people aged 14 - 16 years old can be cared for (even if only occasionally) on most wards that are generally regarded as adult wards with the obvious exceptions of wards like Care of the Elderly. Staff in those locations will be made aware of the training opportunities mentioned in 8.3 and 8.3.1.

BHSCT Service groups will consider cohorting young people in dedicated wards - where this can be done safely and will not lead to any diminution in the level of care.

8.3.5 The BHSCT will work with the NIMDTA to ensure that the principles of paediatric fluid therapy and its potential risks, as highlighted in the National Patient Safety Agency Alert, are highlighted in postgraduate training programmes.

8.3.6 All professionals caring for children must be able to diagnose and manage acute hypoglycaemia.

8.4 *NPSA 4 RQIA 11* Fluid prescription/ balance chart

A new fluid prescription/ balance chart has been developed within the Royal Belfast Hospital for Sick Children (RBHSC) with guidance from all other areas in the BHSCT that treat children. It will be used for the prescription of fluids for all children and young people treated in the BHSCT with the exception of treatment of diabetic ketoacidosis (DKA) when a specialised fluid prescription chart may be used.

If needed, they should avail themselves of advice from the sources as detailed in Appendix 5.

8.4.1 All children, other than emergencies, must have a blood sample taken for electrolyte and blood glucose estimation before intravenous maintenance fluids are started. This must be repeated at least 24 hourly, more often in the circumstances described. Clinical and other methods of monitoring are outlined in the guidance.

8.4.2 Monitoring

Monitoring of the child receiving parenteral fluid will include considerations of:-

- Body weight to be measured or assessed as a baseline and at least daily thereafter.
- Clinical state to be closely monitored and recorded on a regular basis.
- All fluid intake of any kind (intravenous, oral and medicines) must be measured and recorded on the fluid balance chart.
- All fluid output must be assessed and, if clinically indicated, measured and recorded on the fluid balance chart.
- An assessment of input/output and need for plasma glucose estimation should be made and documented every 12 hours.
- A formal reassessment of the fluid prescription and the need for intravenous fluids must be made and documented every 12 hours.
- Measurement of E&U and blood glucose/BM should be made at least daily.
- If hyponatraemia exists, these measurements should be 4 – 6 hourly.
- Urinary osmolarity and electrolytes measurements should be considered when dealing with hyponatraemia.
- The ill child will require more frequent and detailed investigations.

For more detailed information about the monitoring requirements the wallchart[2] should be consulted.

8.5 **Audit**

NPSA 5 RQIA 12 The BHSCT will implement the following governance measures.

8.5.1 *NPSA 5 RQIA 13* The BHSCT clinical biochemistry department will collate, analyse and report quarterly on paediatric hyponatraemia incidents to designated clinicians for children and young people. They will regularly audit these incidents, collate them with the Trust Adverse Incident Reporting System and instigate actions linked to the NPSA Alert 22. Appendix 3 outlines this audit process.

8.5.2 Incident reporting

NPSA 5 RQIA 14 The BHSCT will report these potential adverse incidents related to intravenous infusion through the Trust Adverse Incident Reporting System.

A system of 'triggers' (adapted from those developed by the NHSCT) will be used to

- generate a list of hospital acquired hyponatraemia episodes
- highlight variance from best practice guidance as highlighted in this document
- generate a Trust Adverse Incident Form whenever such incidents occur.

These triggers (Appendix 3) will cover the choice of fluid prescribed at ward level, charting relevant findings in the medical notes, the frequency of electrolyte analysis and the detection of biochemical abnormalities.

8.5.3 Audit

NPSA 5 RQIA 15,16 The BHSCT will implement an audit programme for intravenous infusion therapy in children throughout the trust.

The audits will be based on the

- NPSA audit checklist
  http://www.npsa.nhs.uk/EasySiteWeb/GatewayLink.aspx?alId=5308
- the BHSCT trigger list (Appendix 3).
- Regional GAIN hyponatraemia audit

8.5.4 Where young people are cared for in general adult wards, special audit arrangements will be put in place to ensure they receive appropriate and safe fluid management.

9. Additional policy statements:

9.1 Senior medical advice must be sought when treating the child with hyponatraemia.

9.2 Where additional electrolytes are required, they should only be administered as supplied by the manufacturer and in line with guidance.

Children at or below the age of 13 years must not have electrolytes added to bags of intravenous fluids.

Ordinarily children from 13 to 16 should also not have electrolytes added to bags of intravenous fluids; in certain, predominantly adult areas, children of this age group may have magnesium sulphate or phosphates added.

9.3 Apart from boluses for shocked patients, fluids may only be administered by way of an infusion device. Details of the pump must be recorded on the fluid prescription and balance chart.

9.4 When referring to this policy, staff should consult the BHSCT policy on the management of strong intravenous potassium solutions and/or injections.

10. Implementation / Resource requirements:

The implementation requirements for this policy include:-

- Wallchart production and distribution
- Fluid prescription/ balance chart production and distribution
- Staff training costs – induction, postgraduate courses.

Raising staff awareness of the issues surrounding hyponatraemia and the subsequent staff training will be encouraged, as suggested by DHSSPSNI circular[4], by using the BMJ e-learning module.

11. Source(s) / Evidence Base:

The following sources were used:-

a) NPSA Alert 22
b) NPSA background information
   http://www.npsa.nhs.uk/EasySiteWeb/GatewayLink.aspx?alId=5310
c) HSC (SQSD) 20-07 - reducing risk of Hyponatraemia in children (27/04/2007)
d) HSC (SQSD) 20-07 - addendum (16/10/2007)
e) Paediatric Parenteral Fluid Therapy wallchart.

12. References, including relevant external guidelines:

1. Reducing the risk of hyponatraemia when administering intravenous infusions to children. National Patient Safety Agency, Patient Safety Alert 22, March 2007.
2. Paediatric Parenteral Fluid Therapy initial management guideline, DHSSPSNI 2007. http://www.dhsspsni.gov.uk/hsc_sqsd_20-07_wallchart.pdf.
3. HSC (SQSD) 20-07 reducing risk of Hyponatraemia in children
4. http://www.dhsspsni.gov.uk/hsc_sqsd_20-07_-_addendum.pdf

5. Regulation and Quality Improvement Authority (RQIA). Reducing the risk of hyponatraemia when administering intravenous infusions to children - September 2008. http://www.rqia.org.uk/cms_resources/NI%20%20report%20Hyponatraemia%20FINAL%20v%203%200.pdf

13. Consultation Process:

This policy is adapted from the

- NPSA Alert 22,
- Northern Ireland Regional Paediatric Fluid Therapy Working Group
- HSC (SQS) 20/2007 and its addendum documentation from the DHSSPSNI.

It has been assured through the Standards and Guidelines committee.

14. Equality and Human Rights screening carried out:

In line with duties under the equality legislation (Section 75 of the Northern Ireland Act 1998), Targeting Social Need Initiative, Disability discrimination and the Human Rights Act 1998, the Belfast Trust has carried out an initial screening exercise to ascertain if this policy should be subject to a full impact assessment.

√ Screening completed ☐ Full impact assessment to be carried out.
No action required.

15. Procedures:

Appendix 1 - Paediatric Parenteral Fluid Therapy wallchart
Appendix 2 - Estimating the percentage dehydration based upon physical examination findings.
Appendix 3 - Paediatric Hospital Acquired Hyponatraemia Audit
- Triggers for potential adverse events
Appendix 4 - Availability of intravenous fluids throughout the BHSCT (500ml bags)
Appendix 5 - Sources of advice regarding Paediatric fluid therapy
Appendix 6 - Areas where it is permitted to stock/order No. 18 Solution* - as of August 2009
Appendix 7 - RQIA independent review - September 2008 - Recommendations

Director **Author**

Date: **Date:**

Appendix 2

Estimating the percentage dehydration based upon physical examination findings.

Estimated Percentage Dehydration	Physical Examination Findings
<3	History of fluid loss but no findings on physical examination
5	Dry oral mucous membranes but no panting or pathological tachycardia
7	Mild to moderate decreased skin turgor, dry oral mucous membranes, slight tachycardia, and normal pulse pressure.
10	Moderate to marked degree of decreased skin turgor, dry oral mucous membranes, tachycardia, and decreased pulse pressure.
12	Marked loss of skin turgor, dry oral mucous membranes, and significant signs of shock, pallor, cool peripheries, prolonged capillary refill time, hypotension, confusion.

Appendix 3

PAEDIATRIC HOSPITAL ACQUIRED HYPONATRAEMIA AUDIT

Laboratory Report Details (to be completed by audit dept)

Patient No. Patient Date of Birth:

Date of specimen: Time of specimen: Result :

Admission Details

Date of admission: Time of admission:

Diagnosis: 1.

2.

Hospital acquired hyponatramia (defn)

- Na ≥130mmol/l at time of admission, & a subsequent Na of < 130mmol/l whilst on IV fluids.
- Na< 130mmol/l on their initial U&E's, where the U&E's are done >48hrs after admission and they are on IV fluids.
- Admitted from another hospital with Na < 130mmol/l at time of admission whilst on IV fluids.

1. Is this hospital acquired hyponatraemia? Yes / No

   If no, reason: _____

   If yes, was it acquired whilst in this trust? Yes / No

   If no, patient transferred from: _____

Treatment and monitoring of hyponatraemia

2. Was the fluid prescribed appropriate? Yes / No

   If no, details: _____

3. Was IV fluid prescription reviewed 12hrly whilst on IV fluids? Yes / No

4. Were U&E done 24hrly whilst on IV fluids? Yes / No

Following the Na of <130mmol/l,

5. Was appropriate advice sought? Yes / No

   Grade: _____ Speciality: _____

6. Was the frequency of repeat U&Es appropriate? Yes / No

   If No, details: _____

Recording and communication of incidents (to be completed by Audit dept)

7. If yes to Q1, was adverse incident form completed? Yes / No

8. Was copy of form sent to other trust if acquired outside BHSCT? Yes / No

Triggers for potential adverse events related to the administration of intravenous fluids to children (1 month – 16 years old)

(adapted from Northern H&SCT policy)

CHOICE OF IV FLUID

1. Bolus fluid: use of a solution with sodium concentration of <131mmol/L for treatment of shock.
2. Deficit fluid: use of a solution with sodium concentration of <131mmol/L for correction.
3. Maintenance fluid: use of a solution with sodium concentration of <131mmol/L in a peri-operative patient (intraoperative period and first 24 hours following surgery).

BIOCHEMICAL ABNORMALITIES

4. Any episode of symptomatic hyponatraemia while in receipt of IV fluids.
5. Any episode of hypoglycaemia (blood glucose less than 3mmol/L) while in receipt of IV fluids.
6. Any episode of severe acute hyponatraemia (i.e. sodium level dropping from 135mmol/L or above to < 130mmol/L within 24hrs of starting IV treatment).

ASSESSMENT

7. Electrolytes not checked at least once per 24 hours in any patient receiving IV fluids exclusively.
8. Failure to record the calculations for fluid requirements on the prescription sheet.
9. Failure to note in the case notes/ prescription sheet a serum sodium of less than 130mmol/L.
10. Failure to document in the case notes the steps taken to correct a serum sodium of less than 130mmol/L.

If any of the above occurs an IR1 Form must be completed.

October 2010

Appendix 4

AVAILABILITY OF INTRAVENOUS FLUIDS THROUGHOUT THE BHSCT (500ML BAGS)

SITE	RGH	BCH	MPH	MATER
Sodium chloride				
Sodium chloride 0.45%	√	√		√
Sodium chloride 0.9%	√	√	√	√
Sodium chloride 1.8%	√	√	√	√
Sodium chloride 2.7%	√		√	√
Combined solutions				
Sodium chloride 0.45% Glucose 2.5%	√	√	√	
Sodium chloride 0.45% Glucose 5%	√		√	
Sodium chloride 0.9% Glucose 5%	√			
Glucose solutions				
Glucose 5%	√	√	√	√
Glucose 10%	√	√	√	√
Glucose 15%	√			
Glucose 20%	√	√		
Potassium containing solutions				
Glucose 5% 10mmol Potassium chloride	√			
Glucose 5% 20mmol Potassium chloride	√	√	√	
Glucose 5% 40mmol Potassium chloride	√	√	√	
Glucose 10% 10mmol Potassium chloride	√			√
Glucose 10% Sodium chloride 0.18% 10mmol Potassium chloride*	√			
Sodium chloride 0.45% Glucose 2.5% 10mmol Potassium chloride	√	√		
Sodium chloride 0.45% Glucose 2.5% 20mmol Potassium chloride	√			
Sodium chloride 0.45% Glucose 5% 10mmol Potassium chloride	√			
Sodium chloride 0.45% Glucose 5% 20mmol Potassium chloride	√			
Sodium chloride 0.9% 10mmol Potassium chloride	√			
Sodium chloride 0.9% 20mmol potassium chloride	√	√	√	√
Sodium chloride 0.9% 40mmol potassium chloride	√	√		

* commonly known as Basic solution

Sites: RGH = Royal Hospitals
BCH = Belfast City Hospital
MPH = Musgrave Park Hospital
MATER = Mater Hospital

Appendix 5

Sources of advice regarding Paediatric fluid therapy

For help and advice regarding

- management of fluid therapy
- especially to prevent and/or treat hyponatraemia

in all children, but especially for those children aged 13 – 16 years old being managed in adult wards,

please use the following sources of help and advice. Ordinarily, advice should be for complex cases and should be Consultant to Consultant discussions even though contact will often have to be made through trainee on-call rotas.

Team		Address	Extension
RBHSC Paediatricians	Paediatric On Call Rota	Allen Ward Musgrave Ward	Bleep 2277
RBHSC Paediatric ICU	Paediatric ICU		2449
Musgrave Park	Orthopaedic theatre – Anaesthesia team during working hours.		
BCH Dufferin theatres	ENT theatre – Anaesthesia team during working hours.		
General Biochemistry	**Clinical Biochemistry**		
	Inside working hours	**Outside working hours**	
RVH Tie line:7222 Ext.3798	Ext.4714	Contact Medical doctor on call either via the laboratory or via switchboard.	
BCH Tie line:7111 Ext. 3096/2926/3628	Ext.3497/3136/3160	Ext.3216 or Contact Medical doctor on call either via the laboratory or via switchboard	
MIH Tie line: 7231 Ext. 2223/2229	Ext.2326/2228	Contact Medical doctor on call either via the laboratory or via switchboard	

Other sources of help are:

1 APA consensus guideline on perioperative fluid management in Children
http://www.apagbi.org.uk/docs/Perioperative_Fluid_Management_2007.pdf

2 Royal Children's hospital Melbourne Clinical Practice Guidelines
Intravenous fluids
http://www.rch.org.au/clinicalguide/cpg.cfm?doc_id=5203#Other%20Resources

3 Royal Children's hospital Melbourne Clinical Practice Guidelines
Hyponatraemia
http://www.rch.org.au/clinicalguide/cpg.cfm?doc_id=8348

Appendix 6

Areas where it is permitted to stock/order No. 18 Solution* - as of August 2009

SERVICE GROUP	SITE	SPECIALITY	Stock on Ward	Named patient supply – consultant request only.
Clinical Services	RGH, BCH	High Dependency Unit	X	
Clinical Services	RGH, BCH, MATER	Intensive Care	X	
Clinical Services	Mater, BCH, RGH	Recovery Wards		X
Clinical Services	Mater, RGH	Theatres		X
Clinical Services	BCH	Tower Theatres		X
Clinical Services / OPMS	Mater, RGH, BCH	Day Procedure Units		X
Specialist Serv	RGH	Wards 4E and 4F (Neurosciences)		X
OPMS T&O	MPH	Recovery Ward - Orthopaedics		X
OPMS T&O	MPH	High Dependency Unit		X
OPMS T&O	MPH	Theatres - Orthopaedics		X
SS, Women, family and childcare	RBHSC	Barbour Renal	X	
SS, Women, family and childcare	RBHSC	PICU	X	

* "No. 18 Solution" = sodium chloride 0.18% and glucose 4%

Appendix 7

RQIA INDEPENDENT REVIEW - SEPTEMBER 2008 - RECOMMENDATIONS

Recommendation 1	All hospitals should monitor the ongoing use of No. 18 solution to enable assurance that infusions are removed from stock and general use in areas that treat children.
Recommendation 2	Where appropriate, hospitals must be able to demonstrate that an active strategy is in place for minimising risk of use in clinical areas that continue to stock No 18 solution and where children are accommodated. For example, provision of additional labelling or separate storage for those No.18 solution bags still stocked in such clinical areas.
Recommendation 3	All hospitals should continue with the ongoing work of disseminating clinical guidelines. This should be undertaken in conjunction with multidisciplinary awareness-raising and education on the use of the guidance and wall chart in all settings where children may be treated. This is particularly important in adult wards where older children are treated.
Recommendation 4	Independent hospitals must be assured that all visiting doctors who may manage patients up to 16 years old use the clinical guidelines when managing children being treated with intravenous infusions.
Recommendation 5	All hospitals should ensure that only the DHSSPS Paediatric Parenteral Fluid Therapy wall-chart *issued by DHSSPS in October 2007* is displayed in clinical areas where children may be treated, with a list of available local fluids available alongside it. All previous versions of the wall chart should be removed from clinical areas.
Recommendation 6	Hospitals should assure themselves that staff have the appropriate skill and knowledge in this clinical area. Competency assessment tools in administration of intravenous infusion to children should be developed, formalised and implemented for all relevant, multi-professional staff.
Recommendation 7	Hospitals should continue to review, collaborate and implement organisation wide policy and guidelines, in relation to intravenous infusion for children.
Recommendation 8	All hospitals should ensure that the development and provision of multidisciplinary education opportunities in administration of intravenous infusion to children and that all relevant clinical staff uptake this education.
Recommendation 9	Hospitals should develop mechanisms to identify the location of patients aged 14-16 years who are in adult wards and ensure staff who care for those children are provided with competency based, assessed education in administration of intravenous infusion to children.
Recommendation 10	All hospitals should make wider use of training sources available such as BMJ E-Learning Module on Hyponatraemia to address different learning styles and devise a mechanism to ensure 100% multi-professional uptake of such learning.
Recommendation 11	Priority must be given to the completion of a Trust-wide review, and implementation of revised paediatric intravenous fluid prescription and

fluid balance charts in all settings where children may be treated including adult wards where children are treated.

Recommendation 12 All hospitals should develop a culture of incident reporting, analysis and learning generally and specifically in respect of intravenous fluids and hyponatraemia.

Recommendation 13 Plans for development of systems for reporting, analysing and monitoring incidents to assure organisations of safe practice and that actions linked to NPSA Alert 22 should be implemented and regularly audited by all hospitals to ensure adherence to the process.

Recommendation 14 The development of 'trigger lists' that have been adopted by a the Antrim Area Hospital to aid understanding of the types of incidents to be reported should be shared and taken up more widely .

Recommendation 15 The development of an audit tool which may include wider aspects but should address as a minimum aspects of NPSA Alert 22 should continue to be progressed and used at least annually.

Recommendation 16 Trusts should continue to seek approval and funding for a regional audit (GAIN proposal) on the uptake of the Paediatric Parenteral Fluid Therapy guideline and potential unexpected clinical consequences of the guideline.

PAEDIATRIC PARENTERAL FLUID THERAPY (1 month – 16 yrs)

Initial management guideline

Sept 2007

Monitoring & observations essential

ALL CHILDREN

Admission Weight, U&E *(unless child is well & for elective surgery)*

12 Hourly –
Assess In / Output, plasma glucose

Daily – Clinical reassessment. U&E (more often if abnormal; 4-6 hourly if Na^+ < 130 mmol/L).

ILL CHILDREN
May need:
Hourly - HR, RR, BP, GCS. Fluid In/ Output (urine osmolarity if volume cannot be assessed)
2-4 hourly – glucose, U&E, +/- blood gas.

Daily – weight if possible

Each shift
Handover and review of fluid management plan.

If plasma Na^+ < 130 mmol/L or > 160 mmol/L or plasma Na^+ changes > 5 mmol/L in 24 hours ask for senior advice

Is shock present?

YES

ADMINISTER RAPID FLUID BOLUS
Give 20 ml/kg sodium chloride 0.9% IV or intraosseous
[10 ml/kg if history of haemorrhage or in diabetic ketoacidosis]
Reassess. Repeat bolus if needed. Call for senior help.
(Up to 60 ml/kg may be needed. Use blood after 40 ml/kg if patient has haemorrhaged)

NO

Can child be managed with oral fluids?

YES

PRESCRIBE ORAL REHYDRATION SOLUTION

DKA / burns: initiate departmental protocol. Renal / cardiac / hepatic - get senior advice.

Is there a fluid deficit?

YES

ESTIMATE DEFICIT
FLUID DEFICIT = (% dehydration x kg x 10) as mls of:
sodium chloride 0.9%
The volume of fluid to be prescribed is: fluid deficit MINUS volume of any fluid bolus received
Prescribe this residual volume of deficit separately from the maintenance prescription.
Give over 24 hours (but over 48 hours if Na^+ < 135 or > 145 mmol/L)
ONGOING LOSSES: calculate at least 4 hourly. Replace with an equal volume of:
sodium chloride 0.9% (with or without pre-added potassium)
Be prepared to change fluid type and volume according to clinical reassessment, electrolyte losses and test results

NO

Prescribe Maintenance fluids

CALCULATION OF 100% MAINTENANCE RATE

(a) for first 10 kg:	100 ml/kg/ day	=	4ml/kg/hr
(b) for second 10 kg:	50 ml/kg/ day	=	2ml/kg/hr
(c) for each kg over 20 kg:	20 ml/kg/ day	=	1ml/kg/hr

[for 100% daily maintenance add together (a) + (b) + (c)]

MAXIMUM: in females 80 mls per hour; in males 100 mls per hour
If risk of hyponatraemia is high consider initially reducing maintenance volume to two thirds of maintenance

PRESCRIBE INITIAL IV MAINTENANCE FLUID AND TIME FOR REASSESSMENT

Patients particularly at risk of hyponatraemic complications:
peri-operative patients; patients with head injuries; gastric losses; CNS infection; severe sepsis; hypotension; intravascular volume depletion; bronchiolitis; gastroenteritis with dehydration; abnormal plasma sodium, particularly if less than 138 mmol/L but also when greater than 160 mmol/L; salt wasting syndromes.

Fluid choices: glucose containing fluid normally required if under 1 year old and may also be required by older children

sodium chloride 0.9% (with/ without pre-added glucose 5%)
or
Hartmann's Solution
or
Solution Corporately Approved at Trust Level

Other Patients:
sodium chloride 0.45% with pre-added glucose 2.5% or 5%

All Patients:
Alter fluid rate according to clinical assessment. Change electrolyte and glucose content of infusion fluid according to test results.
COMMENCE ORAL FLUIDS & DISCONTINUE IV FLUIDS AS SOON AS POSSIBLE

Hypokalaemia (< 3.5 mmol/L): Check for initial deficit. Maintenance up to 40 mmol/L IV potassium usually needed after 24 hrs using pre-prepared potassium infusions as far as possible. Consult Trust Policy on IV strong potassium.
Oral intake and Medications: volumes of intake, medications & drug infusions must be considered in the fluid prescription.
Hypoglycaemia (< 3 mmol/L). Medical Emergency: give 5 ml/kg bolus of glucose 10%. Review maintenance fluid, consult with senior and recheck level after 15-30 mins. **INTRA-OPERATIVE PATIENTS:** consider monitoring plasma glucose.
Symptomatic Hyponatraemia: check U&E if patient developes nausea, vomiting, headache, irritability, altered level of consciousness, seizures or apnoea. This is a Medical Emergency and must be corrected.
Commence infusion of sodium chloride 2.7% at 2 ml/kg/hour initially and get senior advice immediately.

Standards & Guidelines Committee – Hyponatraemia + IV fluids for children – V3.6 – 17/09/2009

PAEDIATRIC PARENTERAL FLUID THERAPY (1 month – 16 yrs)

Initial management guideline

Sept 2007

Monitoring & observations essential

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2-4 hourly – glucose, U&E, +/- blood gas.

Daily – weight if possible

Each shift

Handover and review of fluid management plan.

If plasma Na^+ < 130 mmol/L or > 160 mmol/L or plasma Na^+ changes > 5 mmol/L in 24 hours ask for senior advice

Is shock present? YES →

ADMINISTER RAPID FLUID BOLUS
Give 20 ml/kg sodium chloride 0.9% IV or Intraosseous
[10 ml/kg if history of haemorrhage or in diabetic ketoacidosis]
Reassess. Repeat bolus if needed. Call for senior help.
(Up to 60 ml/kg may be needed. Use blood after 40 ml/kg if patient has haemorrhaged)

NO ↓

Can child be managed with oral fluids? YES →

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DKA / burns: initiate departmental protocol. Renal / cardiac / hepatic - get senior advice.

Is there a fluid deficit? YES →

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FLUID DEFICIT = (% dehydration x kg x 10) as mls of:
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The volume of fluid to be prescribed is: fluid deficit MINUS volume of any fluid bolus received

Prescribe this residual volume of deficit separately from the maintenance prescription.
Give over 24 hours (but over 48 hours if Na^+ < 135 or > 145 mmol/L)

ONGOING LOSSES: calculate at least 4 hourly. Replace with an equal volume of:
sodium chloride 0.9% (with or without pre-added potassium)

Be prepared to change fluid type and volume according to clinical reassessment, electrolyte losses and test results

NO ↓

Prescribe Maintenance fluids →

PRESCRIBE INITIAL IV MAINTENANCE FLUID AND TIME FOR REASSESSMENT

Patients particularly at risk of hyponatraemic complications:
peri-operative patients; patients with head injuries; gastric losses; CNS infection; severe sepsis; hypotension; intravascular volume depletion; bronchiolitis; gastroenteritis with dehydration; abnormal plasma sodium, particularly if less than 138 mmol/L but also when greater than 160 mmol/L; salt wasting syndromes.

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sodium chloride 0.9% (with/ without pre-added glucose 5%)
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(c) for each kg over 20 kg:	20 ml/kg/ day	= 1ml/kg/hr

[for 100% daily maintenance add together (a) + (b) + (c)]

MAXIMUM: in females 80 mls per hour; in males 100 mls per hour

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499

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The outcome of pediatric cadaveric renal transplantation in the UK and Eire

Postlethwaite RJ, Johnson RJ, Armstrong S, Belger MA, Fuggle SV, Martin S, Middleton D, Ray TC, Rigden SPA, Verrier-Jones K, Morris PJ, on behalf of the Paediatric Task Force of United Kingdom Transplant, Bristol. The outcome of pediatric cadaveric renal transplantation in the UK and Eire.
Pediatr Transplantation 2002: 6: 367–377. © 2002 Blackwell Munksgaard

Abstract: An analysis of all pediatric cadaveric renal transplant recipients in the UK and Eire was undertaken to review the outcomes of pediatric cadaveric renal transplantation and to consider the implications for organ allocation procedures for pediatric recipients. Factors influencing the outcome of 1,252 pediatric cadaveric renal transplants in the UK and Eire in the 10-yr period from 1 January 1986 to 31 December 1995 were analyzed by Cox proportional hazards regression, including analysis of four distinct post-transplant epochs (0–3 months, 3–12 months, 12–36 months, and beyond 36 months). At the time of analysis (December 2000), 113 (11%) recipients had died and 47% of grafts had failed. In the multi-factorial modelling, the factors significantly affecting transplant outcome were cold ischaemia time, donor and recipient age and human leucocyte antigen (HLA) matching. Epoch analysis demonstrated that these factors operated at different times post-transplant. Cold ischaemia time had a strong influence on outcome at 3 months. A highly significant increased risk of graft failure was associated with donors under 5 yr of age. Young recipients had an increased risk of failure in the short term, but beyond 1 yr post-transplant there were few failures in young recipients while a steady rate of graft loss persisted in the older children. In terms of HLA matching, the worst outcome was observed for two HLA-DR mismatched grafts, while 000 and favorably matched kidneys (100, 010, 110 HLA-A, -B, -DR mismatches) survived longest. Hence, a policy of exchanging organs on the basis of HLA matching is justified for 000 mismatched and favorably matched kidneys. The poor outcome associated with very young donors should discourage pediatric units from transplanting kidneys from such young donors. The reasons for late losses in older recipients need investigation.

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Key words: pediatric cadaveric renal transplantation – renal transplantation outcome – graft failure – causes of death – center effect – HLA matching – donor age – recipient age

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An analysis of the outcome of primary cadaveric renal transplantation in adults in the UK resulted in a revision of the allocation procedures for adult recipients to maximize the transplantation of HLA-matched kidneys, as well as to take account of factors such as waiting time and matchability of the recipient (1). A later report from the USA has similarly concluded that 'a superior graft outcome with little increase in the duration of cold ischaemia time justifies national sharing of HLA-matched kidneys' (2).

The annual reports of the European Dialysis and Transplant Association included outcomes of pediatric renal transplantation and by 1989 had information on 2,113 pediatric renal transplants (3). The most recent systematic data on outcomes in pediatric transplantation comes

Abbreviations: CD, cadaveric donor; CI, confidence interval; CMV, cytomegalovirus; HLA, human leucocyte antigen; LRD, living-related donor; NAPRTCS, North American Pediatric Renal Transplant Cooperative Study; RR, relative risk; UKT, UK Transplant; UNOS, United Network for Organ Sharing.

from North America, particularly from the NAPRTCS registry (4–6) and the UNOS registry (7, 8).

Pediatric recipients were specifically excluded from the UK adult study and therefore the Kidney Advisory Group of United Kingdom Transplant Support Service Authority (now reconstituted as UKT) established a task force to review the outcomes of pediatric cadaveric renal transplantation.

Methods

Study cohort

The study cohort comprised all pediatric cadaveric renal transplants performed in the United Kingdom and Republic of Ireland in the 10-yr period from 1 January 1986 to 31 December 1995. A pediatric recipient or donor was defined as under 18 yr of age at the time of transplantation.

During the study period a total of 1,252 kidney-only pediatric CD transplants were performed in 1,070 recipients. Of these transplants, 1,010 (81%) were first grafts and 242 (19%) were re-grafts. For 30 transplants the HLA-DR typing was incomplete and a further two transplant recipients had no follow-up data reported to the UKT by the time of the analysis. Thus, a total of 1,220 transplants are included in the outcome analysis, of which 989 were first grafts and 231 (19%) were re-grafts; 99.6% had 1-yr follow-up data and 98.0% had 5-yr follow-up data.

Factors analyzed

Factors influencing transplant survival times were analyzed on a multi-factorial basis using the proportional hazards regression model introduced by Cox. Donor factors analyzed were age, gender, blood group, cause of death, and CMV status. Recipient factors analyzed were age, gender, ethnic origin, blood group, primary renal disease, CMV status, waiting time, and graft number (primary vs. re-transplant). Other factors analyzed were year of graft, center status (pediatric or non-pediatric), number of transplants per center, cold ischaemia time, kidney exchange (i.e. whether the kidney was used locally or moved to another center), and HLA matching.

HLA matching was based on the broad and split antigens of HLA-A, HLA-B, and HLA-DR, as detailed in the report on adults (1). HLA typing was performed using a standard microcytotoxicity test or DNA typing methods.

In the UK, on the basis of the adult HLA Task Force analysis, HLA matching is considered in three groups: a 000 mismatched kidney has no mismatches at the HLA-A, HLA-B, or HLA-DR loci; a favorably matched kidney has one mismatch at either the HLA-A and/or the HLA-B loci but no mismatch at the HLA-DR locus (100, 010, 110 mismatches); and all other HLA mismatches are grouped together and termed non-favorable (1). Investigation of HLA matching effects for pediatric recipients was not restricted to these groups, but they were used as a framework for analysis.

Data for cold ischaemia time were available for only 706 grafts. Data for CMV status of graft and recipient was available for only 383 grafts, as this information was not routinely collected by UKT for the whole study period and was not available from all centres. Finally, ethnic origin of the recipient was only known for 71% of grafts. Analyses of these factors were carried out on reduced data sets to test for significance in the Cox model. Primary disease was modelled with a missing data category (9%) and data for all other factors were complete.

Centres meeting the British Association for Paediatric Nephrology criteria for comprehensive pediatric renal centres (9) are referred to in this report as 'pediatric centres' and other centres in which pediatric transplantation was performed are referred to as 'non-pediatric centres'. Centres were further designated as low volume (< 50 pediatric cadaveric transplants in the study period), medium volume (51–100) or high volume (> 100).

Detailed information about immunosuppressive regimens was not available but retrospective information about the use of cyclosporin and anti-T-cell antibody induction regimens was collected.

Statistical analysis

For this analysis, transplant survival time was determined by time from transplant to transplant failure, this being the earlier of return to regular dialysis or patient death. Where no failure was reported the survival time was censored at the date of the last follow-up. Follow-up data to December 2000 were included in the analysis. Cox's proportional hazards regression models were used to analyze the combined effect on survival of many factors. All models were stratified by center to allow for inherent center differences. In addition to overall survival, because the influences of different factors on transplant survival varied depending on the time post-transplant, the modelling investigated the influences on survival in different epochs post-transplant: the first 3 months post-transplant, 3–12 months post-transplant, 12–36 months post-transplant, and the time beyond 3 yr post-transplant. Log cumulative hazard plots did not show any deviation from the proportional hazards assumption within each period, and Cox's proportional hazards models were fitted to the data for each of the four epochs.

The results are presented in terms of estimated relative risks of failure for different groups of individuals compared with the risk for a baseline (reference) group. A relative risk of greater or less than 1.0 indicates, respectively, a higher or lower risk than that associated with the baseline group. A 95% CI was calculated for each relative risk. Kaplan-Meier survival curves were used to illustrate the effects of significant factors identified in the multi-factorial analysis. Any associated p-values were derived from a univariate log-rank test; we used a 5% level of significance. All statistical analyses were performed using the SAS software package (version 6.12).

Results

Characteristics of the study cohort and changes over the study period

Primary disease was reported for 974 of the 1,070 patients transplanted. Congenital renal dysplasia (25%), obstructive uropathy (14%), and reflux nephropathy (12%) were the most commonly reported renal diseases.

There was negligible change in recipient age distribution over the 10-yr period. The median recipient age varied by only 2.5 yr, with the minimum median age being 9.5 yr in 1991 and maximum median age being 12 yr in 1986, 1987 and 1990.

Pediatric CD transplants were carried out in 13 pediatric centres and 21 non-pediatric centres. Four pediatric centres were high volume, one was low volume, and the remaining eight medium volume. One-hundred and twenty five CD transplants were performed in 21 non-pediatric centres, with individual centres performing between one and 18 CD transplants over the period of analysis. The median recipient age of those transplanted at pediatric units was significantly lower than those treated in non-pediatric units (11 yr, inter-quartile range 6–14 vs. 16 yr, inter-quartile range 14–17 yr; Wilcoxon test, $p = 0.001$).

In the whole study period only 32 kidneys from donors under 2 yr of age were used, 31 of these occurring in the first 4 yr but with only a single donor in this age range in the 6 yr between 1990 and 1995 (Fig. 1). There was also a progressive reduction in the use of kidneys from donors between the ages of 2 and 5 yr, from 23% ($n = 30$) of donors in 1986 to 6% ($n = 9$) in 1995. The decreasing use of younger donors is clear when comparing median donor ages over the duration of the study. Median donor age has been steadily increasing from 9 yr (inter-quartile range 4–21) in 1986 to 13.5 yr (inter-quartile range 10–20) in 1995 (Wilcoxon test, $p < 0.0001$). This corresponds to a decreasing use of donors younger than 5 yr of age and an increase in the use of donors aged 10–17 yr, from 17% in 1986 to 48% in 1995, although there has been a reduction in the use of donors 18–35 yr of age.

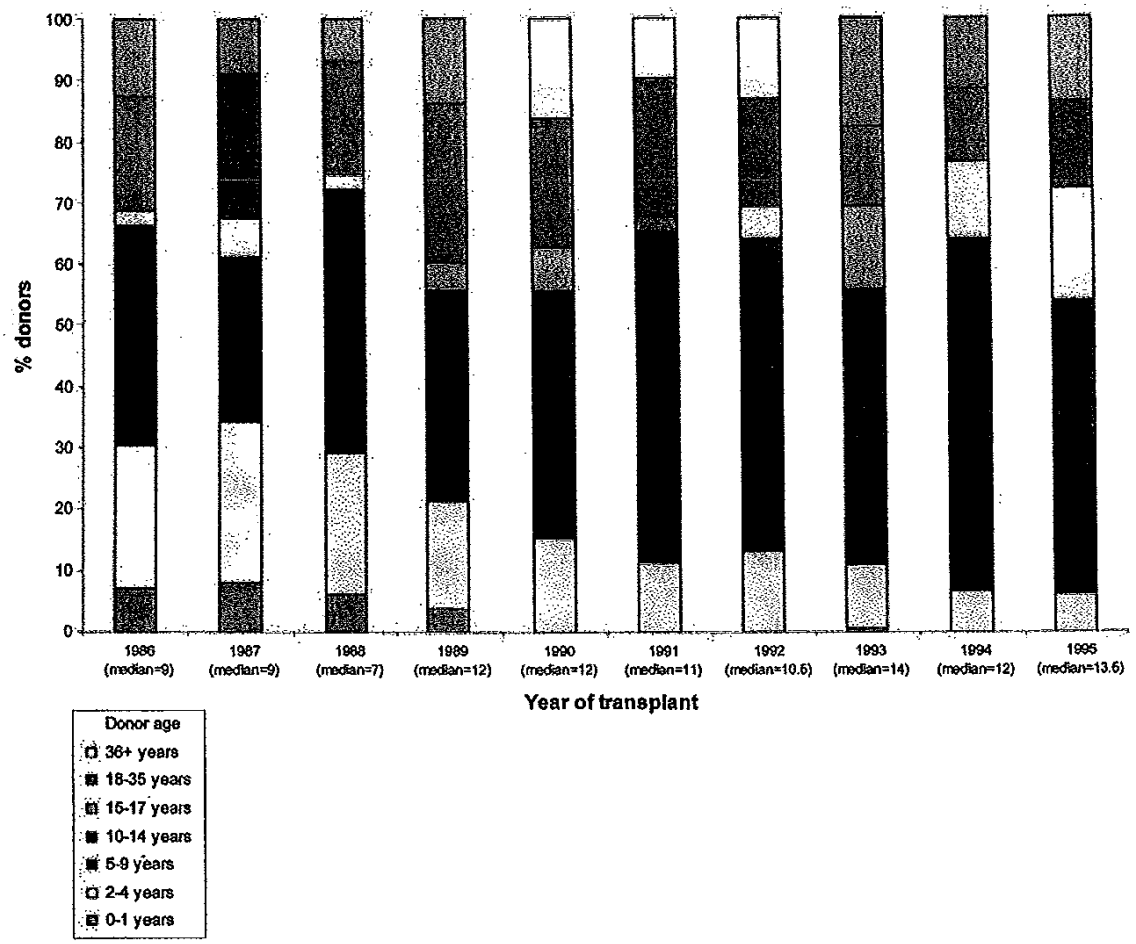

Fig. 1. Donor age by year of transplant.

The degree of HLA-A, -B, and -DR matching has improved substantially during the analysis period (Fig. 2). The proportion of five or six HLA-A + B + DR mismatched grafts has fallen from 18% in 1986 to 1% in 1995. The proportion of all grafts with two DR mismatches has also fallen. In 1986, 27 (23%) transplants were two DR mismatched, of which 15 had a total of five or six HLA-A + B + DR mismatches. In contrast, in 1995, only three transplants were two DR mismatched, of which two had a total of three mismatches and one a total of four mismatches.

One of the 13 pediatric centres did not introduce cyclosporin until 1989, while in all the others cyclosporin was used throughout the study period. Of the 13 pediatric centres, six centres had never used induction anti-lymphocyte antibody regimens. One center used it for second grafts and the other six centres reported occasional use for 'rare cases, such as those with previous aggressive rejection' or 'the occasional "high risk" patient (previous severe rejection/ high cytotoxic antibodies)'. Thus, in the period of analysis, induction regimens with anti-lymphocyte antibodies were rarely used.

Causes of patient death

Of the 1,070 pediatric patients receiving a cadaveric kidney transplant in the study period, 113 (11%) were reported to have died at the time of the analysis. Nine (8%) deaths occurred within 1 month of transplant, 19 (17%) between 1 month and 1 yr of transplant, and 85 deaths (75%) occurred more than 1 yr after transplantation. Thirty-eight (34%) deaths occurred in patients with a functioning transplant. The causes of death are set out in Table 1.

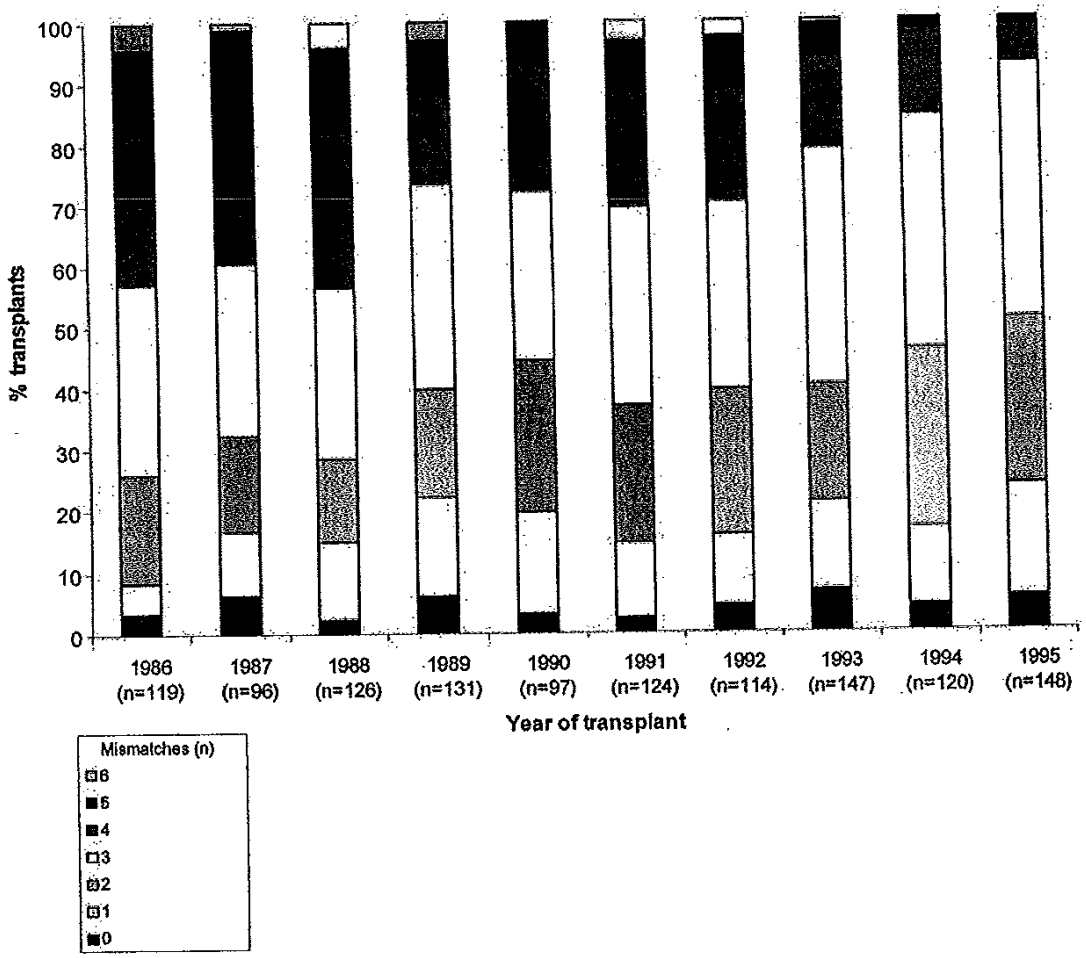

Fig. 2. Number of transplants and human leucocyte antigen (HLA) mismatching by year.

Causes of graft failure

Of the 1,250 transplants with some follow-up information reported, 582 (47%) were reported to have failed by the time of the analysis. A cause of graft failure was given for 500 (86%) of these failures (Table 2). Thirty-two per cent of the graft failures occurred in the first month post-transplant, 10% between 1 month and 3 months, 11% between 3 months and 1 yr, and 47% after 1 yr. Rejection was the commonest cause of graft failure reported (55%). In the first month, however, it only accounted for 38% of losses, with vascular problems accounting for 39%. Recurrent primary disease accounted for only 3% of graft failures, but these losses occurred at all times post-transplant.

Table 1. Cause of death

Cause of death	Number	Percentage of deaths
Infection		
Viral, generalized	1	1
Viral, pulmonary	3	3
Bacterial, pulmonary	2	2
Bacterial, septicaemia	9	8
Other (not viral hepatitis)	1	1
Cardiac failure	9	8
Fluid overload	6	5
Cardiac arrest, cause unknown	9	8
Haemorrhage		
Cerebro-vascular accident	4	4
Gastrointestinal	2	2
From surgery	1	1
From graft site	1	1
Other	2	2
Uraemia due to graft failure	5	4
Patient declined further treatment	1	1
Therapy ceased for other reason	2	2
Cachexia	1	1
Lymphoid malignant disease	4	4
Respiratory failure	4	4
Other identified cause of death	9	8
Intra-operative death	0	0
Accident	3	3
No cause of death reported	34	30
Total	113	

Outcome analysis

Non-significant factors

Graft number was non-significant in relation to transplant outcome, although there were very few third and fourth grafts to analyze.

The CMV status of both donor and recipient (pregraft) and any interaction thereof were found to be non-significant.

Waiting time was also non-significant with relation to transplant survival, but those patients not registered on the national waiting list prior to transplant tended to have poorer outcome in the first 3 months post-transplant.

No center effects could be demonstrated either between individual pediatric centres or comparing pediatric centres with non-pediatric centres or by analysis of center volume.

Other factors found not to significantly relate to graft outcome were recipient; gender, blood group, ethnic origin (based on data with known ethnic origin – 71% of grafts), and primary disease; donor; gender, blood group, and cause of death; and whether the organ was local or imported.

As illustrated by the Kaplan-Meier plot (Fig. 3), graft outcome was significantly better in 1991–95 compared with 1986–90 (Log-rank

Table 2. Cause of graft failure

	Time to failure									
	< 1 month		1 month to < 3 months		3 months to < 1 yr		1 yr +		Total	
Cause of failure	No.	%	No.	%	No.	%	No.	%	No.	%
Hyperacute rejection	8	4	0	0	0	0	2	1	10	2
Rejection while taking immunosuppressive drug(s)	63	34	42	71	39	60	156	57	300	52
Rejection after stopping all immunosuppressive drugs	0	0	1	2	1	2	5	2	7	1
Recurrent primary renal disease	4	2	0	0	4	6	7	3	15	3
Vascular or ureteric operative problems	22	12	1	2	3	5	2	1	28	5
Vascular (arterial or venous) thrombosis	50	27	0	0	0	0	1	0	51	9
Infection of graft	5	3	2	3	1	2	0	0	8	1
Removal of functioning graft	0	0	0	0	1	2	1	0	2	0
'Non-viable' kidney	9	5	4	7	1	2	0	0	14	2
Recipient died, graft was functioning at time of death	4	2	4	7	7	11	23	8	38	7
Other	4	2	2	3	2	3	19	7	27	5
Unknown	16	9	3	5	6	9	57	21	82	14
Total	185		59	100	65	100	273	100	582	

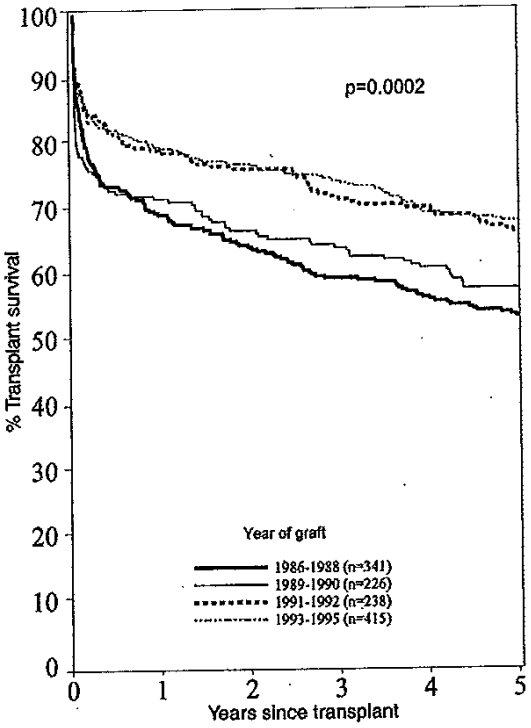

Fig. 3. Transplant survival by year of transplant.

test, p = 0.0002). However, when the effects of increasing donor age and improved HLA matching are taken into account, these fully explain the improvement seen in later years.

Significant factors

In the multi-factorial modelling, the factors significantly related to post-transplant survival were cold ischaemia time, donor and recipient age, and HLA matching. The epoch analysis for 0–3 months, 3–12 months, 12–36 months and after 36 months showed that some factors had differing effects over post-transplant epochs. Table 3 shows results of analysis of overall transplant survival and of the epoch analysis carried out.

There was a trend towards improved transplant survival for grafts with shorter cold ischaemia times (Fig. 4). In the epoch analysis of a reduced data set with known cold ischaemia times (n = 706), cold ischaemia time was shown to have a strong influence in the first 3 months post-transplant, the risk of failure increasing by 4% with each additional hour of cold ischaemia (p = 0.004).

Table 3. Relative risks of transplant failure

			Overall survival			0–3 months			3–12 months			12–36 months			36+ months		
Factor	Level (baseline)	No.	RR	95% CI	p	RR	95% CI	p	RR	95% CI	p	RR	95% CI	p	RR	95% CI	p
Recipient age (years)	0–1	29	0.80	(0.44–1.47)	0.5	1.77	(0.85–3.66)	0.1	0.97	(0.20–4.71)	1.0	0.28	(0.03–2.37)	0.2	–	(–)	–
	2–4	160	0.88	(0.65–1.19)	0.4	1.77	(1.18–2.68)	0.006	0.47	(0.15–1.52)	0.2	0.25	(0.08–0.78)	0.02	0.43	(0.22–0.85)	0.01
	5–9	286	1.05	(0.84–1.32)	0.7	1.77	(1.24–2.51)	0.002	0.98	(0.49–1.94)	0.9	0.38	(0.18–0.78)	0.008	0.77	(0.51–1.16)	0.2
	(10–14)	430	1.00			1.00			1.00			1.00			1.00		
	15–17	315	1.25	(0.99–1.57)	0.06	1.47	(0.99–2.18)	0.05	1.44	(0.77–2.72)	0.3	1.68	(0.99–2.85)	0.05	0.81	(0.54–1.24)	0.3
Donor age (years)	0–1	30	2.77	(1.68–4.58)	<0.0001	3.56	(1.76–7.19)	0.0004	1.34	(0.27–6.58)	0.7	4.16	(0.83–20.88)	0.08	2.58	(0.90–7.40)	0.08
	2–4	179	1.72	(1.25–2.35)	0.0008	2.50	(1.51–4.12)	0.0004	1.22	(0.53–2.83)	0.6	2.24	(0.97–5.17)	0.06	0.87	(0.47–1.60)	0.6
	5–9	290	1.23	(0.91–1.67)	0.2	1.55	(0.94–2.53)	0.08	0.67	(0.29–1.54)	0.3	2.40	(1.17–4.95)	0.02	0.82	(0.48–1.41)	0.5
	10–14	248	1.15	(0.85–1.56)	0.4	1.39	(0.85–2.28)	0.2	0.50	(0.20–1.22)	0.1	1.14	(0.51–2.54)	0.7	1.28	(0.76–2.14)	0.4
	15–17	96	0.91	(0.61–1.37)	0.7	0.73	(0.35–1.53)	0.4	0.14	(0.02–1.08)	0.06	1.58	(0.67–3.71)	0.3	1.30	(0.68–2.50)	0.4
	(18–35)	223	1.00			1.00			1.00			1.00			1.00		
	36+	154	1.48	(1.09–2.02)	0.01	1.31	(0.74–2.29)	0.4	1.40	(0.66–3.00)	0.4	1.13	(0.53–2.42)	0.8	1.98	(1.18–3.35)	0.01
HLA match	Favorable	287	0.65	(0.48–0.88)		0.74	(0.46–1.19)	0.2	0.40	(0.18–0.85)	0.02	1.35	(0.60–3.03)	0.5	0.45	(0.25–0.82)	0.009
	Other 0 DR/1 DR mismatch	777	0.74	(0.59–0.94)	0.01	0.97	(0.68–1.38)	0.9	0.39	(0.21–0.73)	0.003	0.88	(0.43–1.83)	0.7	0.58	(0.35–0.95)	0.03
	(2 DR mismatches)	156	1.00			1.00			1.00			1.00			1.00		

HLA, human leucocyte antigen.

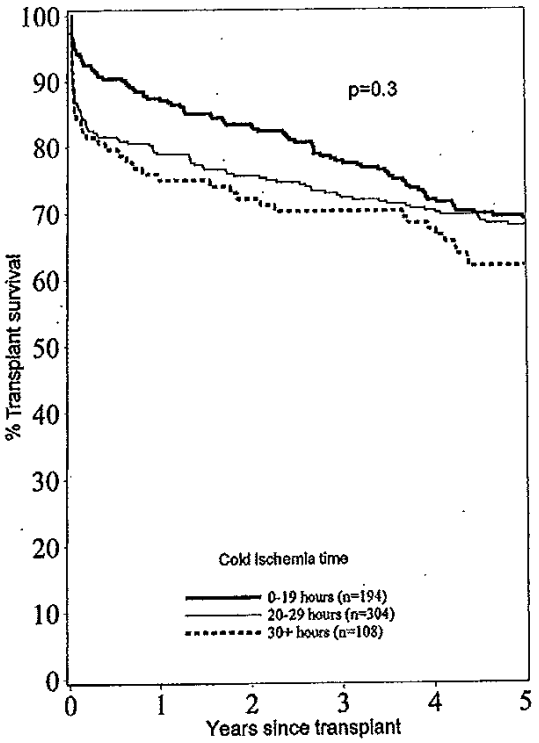

Fig. 4. Transplant survival by cold ischaemia time.

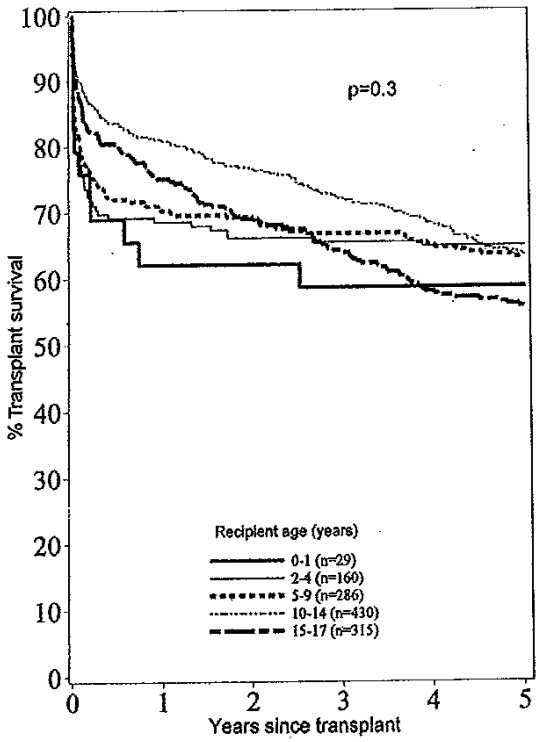

Fig. 5. Transplant survival by recipient age.

In the Cox modelling of distinct post-transplant epochs, the age of both recipient and donor were found to significantly affect post-transplant survival. Owing to differing effects of recipient age on outcome in these epochs, the Kaplan-Meier analysis shows a non-significant effect (log-rank test) on the 5-yr outcome (Fig. 5). The effect of donor age is more consistent across epochs and the Kaplan-Meier analysis shows a highly significant difference between age groups (Fig. 6). Table 3 shows that in the first 3 months after transplantation, recipients aged 10–14 yr of age were least likely to suffer graft failure and for this analysis represent the reference group (see the Methods). Both younger and older recipients had a greater risk of graft loss in the 0–3 months epoch. Between 3 and 12 months this increased risk in young recipients compared with those aged 10–14 yr was lost and young recipients fared better than the reference group in the 12–36 months and 36+ months epochs. In these last two epochs, those aged 10–14 yr or 15–17 yr at transplant were most likely to experience failure of their transplants (Table 3). The effects are illustrated in Fig. 5: for recipients under 10 yr of age at transplant, the survival curves suggest few failures beyond 12 months post-transplant, while the curves for recipients ≥ 10 yr of age show a continuing decline in transplant survival over the 5-yr study period.

The effects of donor age are illustrated in Fig. 6. Donors under 5 yr of age were associated with poor transplant outcome, while the best outcome was associated with transplants from donors 15–17 yr of age. Table 3 shows that the most significant effect of young donor age is in the first 3 months post-transplant. During this time the risk of transplant failure is approximately three times as great when the donor is under 5 yr of age compared with when the donor is 18–35 yr of age (baseline group). Beyond 36 months after receiving a graft, older donors were also associated with increased risk of graft failure compared with the baseline group (RR = 1.98, p = 0.01). We found no significant interaction effect of donor and recipient age.

Figure 7 illustrates transplant survival of the three HLA matching groups found to be most significant in the multi-factorial analysis. The worst outcome was observed for two DR mismatched kidneys, while 000 and favorably matched kidneys were associated with the best transplant outcome. No significant additional benefit for the small number of 000 mismatched

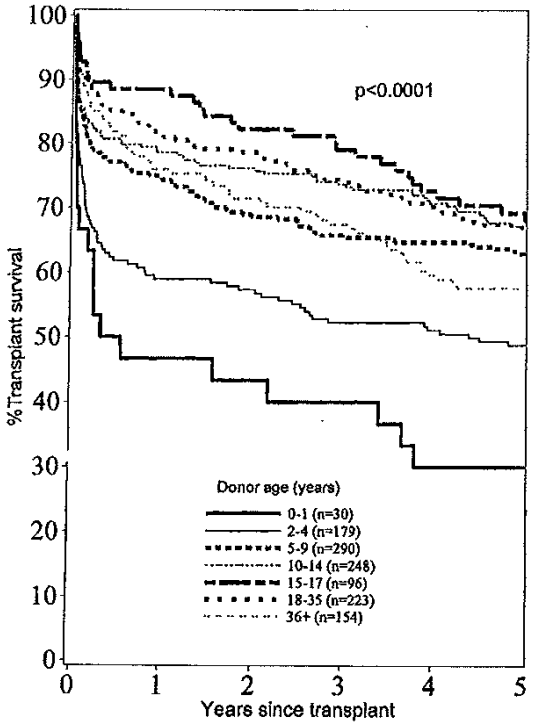

Fig. 6. Transplant survival by donor age.

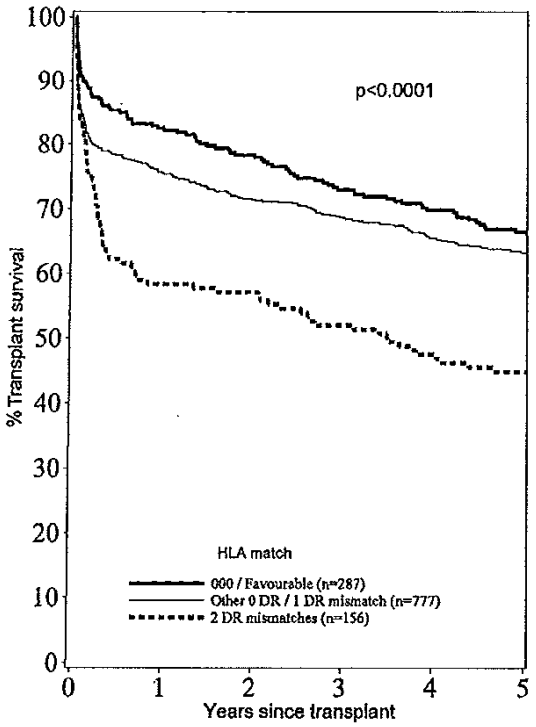

Fig. 7. Transplant survival by human leucocyte antigen (HLA) match grade.

kidneys over favorably matched kidneys could be demonstrated. The multi-factorial analysis showed a weak influence of HLA match in the first 3 months but a stronger effect thereafter. Beyond 36 months, grafts with two HLA-DR mismatches were approximately twice as likely to fail as those with fewer than two mismatches ($p < 0.03$). Even if grafts with causes of failure coded as 'vascular or ureteric operative problems' or 'vascular (arterial or venous) thrombosis' were excluded from the analysis, the effect of HLA matching remained non-significant in the 0–3 months epoch.

Discussion

The influence of donor age on transplant outcome is consistent with a number of reports from registries (4, 5, 10–12) and individual centres (13, 14). Indeed, there seems to be only one report (15) that does not agree with the general finding that outcome worsens progressively with younger donor age. Given the reports of good outcomes in adults with young donor kidneys transplanted en bloc (16–18) this is probably a more appropriate way to utilize the kidneys from young donors. If successful, there is no reason that this could not be extended to pediatric recipients in the future.

The effect of young recipient age is also in agreement with most reports from registries and single centres (4, 5, 10–12). As with donor age, any minimum age criterion for transplantation is, to some extent, arbitrary and the analysis is supportive of the general adoption of 2 yr of age as the minimum age criterion for cadaveric transplantation. However, it is noteworthy that at 5 yr, the outcome for young recipients is as good as that of older recipients, the early poor outcome being offset by better outcome than that seen for older pediatric recipients beyond 1 yr. Therefore, the avoidance of transplantation in patients < 2 yr of age must be viewed as a relative contraindication to cadaveric donation, and transplantation should be considered if there are problems with dialysis. Additionally, it has been reported that outcomes are better with LRD than CD in children under the age of 2 yr (19). The optimal approach to management of those under 2 yr of age with renal failure requires further assessment.

It is possible that the combination of small recipients and small donors has more than an additive effect but we were unable to show this in

our data, probably owing to the small number of such grafts.

The results confirm the impact of HLA matching on transplant outcome in cadaveric donation in children (4, 5, 10). In contrast to the adult study (1), we were unable to show any added advantage of 000 HLA-A, -B, -DR mismatched transplants over favorably matched kidneys, although there were very few of these (n = 55). In addition to inferior transplant survival, another consequence of using poorly matched kidneys in children is increased sensitization to HLA antigens, which makes subsequent transplantation difficult. Data on HLA sensitization for this cohort will be communicated in another report.

The epoch analysis revealed some important effects. The only comparable analysis is that of UNOS where five out of 26 factors accounted for 81% of the variability in long-term graft survival, namely: transplant center, recipient age and race, transplant year, and panel-reactive antibody (8). Most of these issues have already been discussed. There was insufficient information about panel reactivity to use in the multi-factorial analysis but we could show no effect of graft number. The most important finding was the strong effect of recipient age on 5-yr graft survival, with increased risk of loss at 5 yr in patients < 11 yr of age compared with those who were 11–20 yr of age. We confirmed this important finding with recipients ≤ 10 yr of age at transplant doing significantly better than young people 10–18 yr of age. The reason for this is not clear, but the suggestion that non-compliance is probably a factor (8) is plausible. Another possible factor in this inferior outcome is transfer to adult units. Watson has recently reported worryingly high rates of transplant at this time (20). Increased awareness and expertise in recognizing non-compliance and more detailed study of models of transitional care for this vulnerable age group might improve the outcome for these patients.

With longer follow up (> 3 yr), the increased graft loss associated with donors > 35 yr of age is noteworthy. Increased use of much older donors to maximize HLA matching would probably be inadvisable. As with donor age, any cut-off point is to some extent arbitrary; the current national rules for allocation limit donor age for pediatric recipients to 50 yr.

A further finding on epoch analysis was the secondary worsening of outcome for the very youngest donors with > 3 yr of follow-up. There are number of pieces of evidence that suggest antigen-independent mechanisms play a major role in the progression of chronic renal allograft 'rejection' (21) and in some models nephron supply is a major determinant of long-term graft outcome (22). Clearly there are other possible explanations of this late functional decline but, whatever the cause, this is a further argument against the use of very young donors in pediatric cadaveric renal transplantation.

Cold ischaemia time, whilst not affecting overall outcome, did have a significant effect on outcome at 3 months. This is in agreement with the findings in the NAPRTCS study where a cold ischaemia time of > 24 h was one of the variables predictive of the requirement for dialysis for 7 days post-transplant which in itself had a deleterious effect on long-term graft outcome (4, 23). Thus, increased cold ischaemia time does adversely affect graft outcome, but any cut-off such as 24 h is arbitrary, i.e. the shorter the cold ischaemia time the better the outcome.

The overall outcome of transplantation for this group of children has improved significantly over the study period, but the multi-factorial analysis shows that this is entirely explained by reduction in the use of small donors and the improved HLA matching. The adult study showed an improvement in transplant survival additional to that caused by better HLA matching. This was attributed to changes in immunosuppressive therapy (1). The NAPRTCS have shown a similar improvement in pediatric CD outcome, which they attribute to changes in practice, such as judicious use of CD, increased use of prophylactic anti-lymphocyte antibody, and better maintenance immunosuppression (4, 6, 12, 24). Such conclusions need to be supported by multifactorial analysis to uncover the effects of any confounding variables.

We were unable to show any effect of graft number on outcome. This confirms the NAPRTCS findings where the apparent inferior outcome of re-transplants (4) was shown to be entirely caused by the confounding effect of the use of small donors (25).

Similarly, in keeping with the adult study (1), and in contrast to the findings of the NAPRTCS (4, 6) and UNOS (8), we could find no influence of ethnic origin on outcome. The racial mix may explain this. In our data, 88.6% of those with known ethnic origin were White, 9.5% were Asian, 1.7% were Black, and 0.2% were of another ethnic minority group. In American reports, African–American racial origin, but not Hispanic origin, adversely affects outcome (4, 6, 8).

Center effects have long been recognized in adult renal transplantation (26) but this is a result of many factors, with center volume being only one of many possible factors and probably

not the most important (27–31). The results in the adult UK study mirrored these previous studies with variation in survival between centres but with no clear relationship between the number of transplants performed and transplant survival (1). UNOS compared results from 'professional' pediatric centres with those of other centres that transplanted 'only a few children'. Transplant survival was similar in older children in the two types of center but 'survival results of transplants in infants and young children differed, however, and suggested that the more experienced pediatric centres had an advantage with this special group' (7). This difference, however, 'was explained by the more aggressive pursuit of LRD transplants at the "professional" pediatric centers'. In a subsequent UNOS report, center variation was the chief pretransplant factor influencing graft survival at 1 and 5 yr in pediatric renal transplantation (8). However, UNOS was unable to show that center volume or degree of dedicated resources explained this center effect. The NAPRTCS reported that graft survival for both CD and LRD was better at 3 months and 5 yr in the moderate- and high-volume centres compared with the low-volume centres (high volume > 100 transplants, moderate volume 51–100 transplants, and low volume ≤ 50 transplants over an 8-yr period). These differences were not, however, significant and only achieved significance if the use of anti-lymphocyte antibody induction was excluded from the analysis: 'the significance of differences between the low volume and other groups depends upon the inclusion or exclusion of anti-lymphocyte antibody induction as a covariate in the proportional hazards model' (5). We were unable to show any center effects on transplant outcomes.

This report was not primarily concerned with the causes of graft loss and there was no attempt to standardize or verify the reported causes of graft loss. This accounts for obvious inaccuracies such as hyperacute rejection being reported as a cause of late graft loss. Despite these reservations, the overall pattern of causes of graft loss is clear. Not unexpectedly, the pattern of causes of loss varied with time post-transplant. Technical problems (including thrombosis) accounted for 39% of early losses but only 1% of late losses. In the first month, all types of rejection accounted for 38% of losses whereas this rose to 60% of losses after 1 yr. This is consistent with data from the NAPRTCS which show that renal vascular problems, particularly renal vein thrombosis, are major determinants of early graft loss (4–6). A further report from the NAPRTCS showed that recipient age, donor age, CD (vs. LRD), and cold ischaemia time of > 24 h were all associated with vascular thrombosis post-transplant (32). In one report from a single center there were no episodes of vascular thrombosis in 108 consecutive pediatric renal transplants (72% LRD). The authors attribute their excellent results to 'strict adherence to surgical detail, aggressive fluid management in the small child and careful integration of urologic and transplant surgery' (33). Thus, avoiding young donors and recipients, limiting cold ischaemia time and attention to surgical technique and peri-operative care should reduce early graft losses.

The overall mortality rate, not adjusted for duration of follow-up, is significantly higher (10.6%) than that reported by the NAPRTCS (6.5%) (4), but different categorizations and the large number of deaths with no cause of death reported make meaningful comparisons difficult.

In summary, donor and recipient age and HLA matching were the most important determinants of outcome of pediatric cadaveric renal transplantation. Although cold ischaemia time does have an impact on outcome, this is restricted to the first 3 months after transplant and was not significant in long-term outcome. Thus, as with the UK adult analysis, a policy of exchanging organs on the basis of HLA matching is fully justified for 000 mismatched and favorably matched kidneys. In the past children have, in general, received poorer HLA mismatched kidneys than adults. This analysis suggests that HLA matching is equally important for transplants in children and allocation schemes need to consider how HLA matching in children can be improved. In addition, the poor outcome associated with very young donors should discourage pediatric units from transplanting such young kidneys. The effects of recipient age are less clear cut. Age below 2 yr is a relative contraindication to cadaveric transplantation. Five-year follow-up data for patients 10–18 yr of age raises questions about transplantation in this age group and about non-compliance and transfer to adult services. The effects of these factors operate at different times post-transplant and can be obscured unless the analysis takes account of this.

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54a

Viewpoint

Intravenous fluids for seriously ill children: time to reconsider

Trevor Duke, Elizabeth M Molyneux

Intravenous (iv) fluids are used for many sick and injured children. Such fluids generally used are 0·18% or 0·2% saline with 5% dextrose. These fluids are often given at maintenance rates—100 mL/kg for the first 10 kg of bodyweight, 50 mlL/kg for the next 10 kg, and 20 mL/kg for bodyweight exceeding 20 kg.[1] Some standard paediatric texts caution the need to modify maintenance requirements according to disease states, but this specification has been lost in some recent empirical recommendations: for example, WHO now suggests full maintenance fluids for the routine treatment of bacterial meningitis (albeit with a caution about cerebral oedema), with an emphasis on glucose but not sodium content.[2] This is partly based on concerns about dehydration, but there is no strong evidence that this advice is ideal.[3,4] Hypotonic iv fluids given at maintenance rates might be unsafe, especially in hospitals in developing countries where serum sodium concentration often cannot be measured.

The traditional use of hypotonic maintenance fluid in paediatric medicine is based on requirements of normal physiology—eg, if an infant weighing 6 kg receives 0·18% saline fluid for 24 h, they will receive 3 mmol/kg sodium chloride, 100 mL/kg water, and 3·5 mg/kg per minute glucose. These are the amounts of (1) sodium and chloride needed for normal metabolism and growth; (2) water needed by the kidneys to excrete nitrogenous wastes in urine with similar osmolarity to plasma (so that the kidneys do not need to excessively concentrate or dilute urine); and (3) glucose needed to avoid hypoglycaemia and glycogen breakdown. This sounds ideal, but is it? Most healthy people do not drink this much water each day (average for adults is 2·5–3 L), so their kidneys usually concentrate, or if they drink more than usual dilute, their urine. Healthy people are able to excrete large amounts of free water. This is not the case for many children after surgery, or with serious infections.

Large volumes of hypotonic fluid were generally given after surgery, until reports led to recognition that postoperative patients have reduced free-water clearance, and hypotonic saline solutions at maintenance rates or greater put patients at risk of hyponatraemia and encephalopathy—the syndrome of water intoxication.[5–8]

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Children with serious infections share similar pathophysiological mechanisms and risks of adverse neurological outcomes if given hypotonic iv solutions. We outline the pathophysiology of hyponatraemia in acute infections, and argue that the safest empirical iv fluid for most children with serious infections, who cannot take enteral fluids, is 0·9% sodium chloride with dextrose, at rates of infusion that take account of reduced free-water clearance.

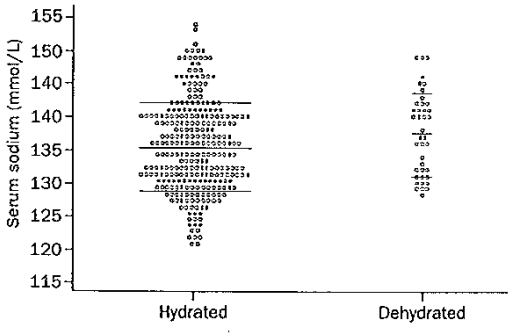
Impaired free-water excretion during severe infections

Antidiuresis during fever and sepsis has been known for over a century, especially in pneumonia and meningitis. Hippocrates' description of pneumonia included scanty and high-coloured urine. In a rhesus monkey model of pneumococcal sepsis, urine volume and free-water clearance decreased to 25% and 17% of baseline values, respectively, during the first 9 h of infection.[9] When 0·45% saline, equal to 105% of urine output in controls, was intravenously infused into septic monkeys, their bodyweight expanded by more than 10% during 9 h of experimental sepsis. Of note, serum sodium concentration or serum osmolarity did not change greatly. In a clinical investigation, 70% of infants with

Mechanism	Setting
Dilution of ECFV	
High ADH activity	Despite normal or expanded ECFV and hypo-osmolarity, so-called SIADH
	Because of hypovolaemia
	Other non-osmotic ADH stimuli[13,17]
	Pain
	Nausea
	Hypoxaemia
	Drugs
	Mechanical ventilation
Increased sensitivity of renal tubules to ADH	Drugs
	Severe illness
Increased intake of free water	Excessive enteral water intake
Iatrogenic administration of free water	iv administration of hypotonic solutions
Increased urinary sodium loss	
ECFV expansion	Retention of free-water from high ADH activity
	Unrestricted oral intake
	Iatrogenic administration
Natriuretic peptide activity (ANP/BNP)	Increased right atrial pressure
Cerebral 'salt wasting'	Described in tuberculous meningitis and traumatic brain injury
Diuretic administration	"
Corticosteroids	"
ADH	ADH may have a direct effect on increasing urinary sodium excretion

ECFV=extracellular fluid volume. ANP=atrial natriuretic peptide. BNP=brain natriuretic peptide. ADH=antidiuretic hormone. SIADH=syndrome of inappropriate ADH secretion.

Table 1: **Causes of hyponatraemia in severe childhood illness**



Serum sodium in well hydrated and dehydrated children with meningitis
p=0·03. Well hydrated, n=286; dehydrated, n=40. Horizontal lines represent mean (SD).

acute bronchiolitis had impaired free-water excretion; at recovery, free-water clearance was up to 15 times more than at the time of admission.[10]

Hyponatraemia in severe infections

Hyponatraemia arises in between 20% and 45% of children with meningitis,[11,12] pneumonia,[13] encephalitis,[14] septicaemia,[15] cerebral malaria,[16,17] and somewhat less often in those with bronchiolitis.[10] The pathophysiological basis is not fully understood, but many factors could be active in the same patient (table 1). Dilution of extracellular fluid because of impaired free-water excretion and increased urinary sodium losses seem to be the main mechanisms. Other mechanisms, including shifts of water from intracellular to extracellular spaces, have been shown in some models of sepsis,[20] but not in others, and are less likely to be important in practice.[21]

Antidiuretic hormone

High concentrations of antidiuretic hormone are seen in many acute febrile illnesses,[22] and are traditionally described as inappropriate. When applied generally, this term indicates our incomplete understanding of the potency of different stimuli to antidiuretic hormone release and suppression (table 1). Hypovolaemia might be a more potent stimulus for secretion of antidiuretic hormone than hypo-osmolarity is to its suppression. In a retrospective study of 300 children with meningitis, investigators noted that serum sodium was lower in those with dehydration than in those with normal hydration.[12] Conversely, a prospective investigation showed that serum sodium concentrations were lower in children with normal hydration than in those with clinical signs of dehydration (figure).[23] Such conflicting data suggest that hyponatraemia arises either as a result of an appropriate pathophysiological response of antidiuretic hormone to restore extracellular fluid volume at the expense of hypo-osmolarity, or as a result of hormonal activity that is inappropriate to both osmolarity and fluid volume status. Antidiuretic hormone also acts centrally, via aquaporin-4 water-transporting proteins expressed in astrocyte foot processes near capillaries and in ependymal cells lining ventricles, to increase brain water.[24,25] Administration of sodium results in a more rapid return to normal of antidiuretic hormone concentrations than does use of low sodium-containing fluid.[4]

Adverse effects of hyponatraemia

In the peripheral circulation, sodium moves freely throughout the extracellular fluid; the hydrostatic pressure gradient and oncotic pressure (predominantly made up of plasma proteins) are responsible for preventing the movement of water out of the vasculature. Cerebral circulation is different. Endothelial tight junctions prevent free movement of sodium across the intact blood-brain barrier, and therefore effective osmolarity is the major determinant of water movement into the brain interstitium or into brain cells.[18] When the blood-brain barrier is intact, an abrupt fall in effective serum osmolarity of 5 mmol/L decreases osmotic pressure difference between the capillary lumen and the brain interstitium by 95 mm Hg (17·5%), favouring water accumulation in the interstitium or brain cells.[26] Many case reports have described acute neurological deterioration in children with serious infections, associated with progressive hyponatraemia and hypotonic intravenous fluid administration (table 2). Researchers who examined the aetiology of extreme hyponatraemia (<115 mmol/L) in a tertiary children's hospital, reported iatrogenic administration of excessive free water as the most common cause.[31]

Investigation	Disease state	Reduction in serum [sodium] or value at time of complication (mmol/L)	Intravenous fluid type and volume	Adverse event	Comments
Cooke[27]	2-year-old girl with tuberculous meningitis	From 130 to 120	Not stated	Coma, seizures	
McJunkin[14]	La Crosse encephalitis (13 of 127 children had neurological deterioration while in hospital)	All children with adverse neurological deterioration had a reduction in sodium. From 138·2 to 134·2 (reduction in mean)	Not stated	Neurological deterioration including cerebral herniation, status epilepticus, and intracranial hypertension	27 children developed hyponatraemia while in hospital, of whom 13 had neurological deterioration
Mor[28]	Infant with pneumonia	107	0·18% saline at 150 mL/kg per day for 2 days	Seizures and cerebral oedema	
Potts[29]	17-month-old with minor burns	From 133 to 113	0·2% saline at 250 mL/kg/day	Seizures	Complications ascribed to SIADH but really represent iv free water intoxication
Jackson[30]	Two children: one with viral respiratory tract infection and one with *Streptococcus pneumoniae* meningitis	121 and 128, respectively, after administration of fluid	5% dextrose at 35–40 mL per kg	Seizures, cerebral oedema, and death	

Table 2: **Adverse events after progressive hyponatraemia induced by hypotonic solutions in children with serious infection or injury**

Fluid	Volume (mL/kg/day)	Volume per day (mL)	Urine output (mL)	Insensible losses (mL)	Total output (mL)	Total net water added (ICF/ECF) (mL)	Na+ added (mmol)	24-h serum [Na]*
0·18% saline	100	600	210	180	390	210 (84/126)	7·2	130·6
0·9% saline	75	450	210	180	390	60 (0/60)	13·5	137·5

Total body water=70% of bodyweight (35% ECF, 35% ICF. ICF=intracellular fluid. ECF=extracellular fluid. Free-water excretion reduced by 50% normal (urine volume from 70–35 mL/kg/day) due to increased activity antidiuretic hormone. Starting serum [Na] 135 mmoL/L; total ECF Na=0·35×6×135=283·5 mmol.
*24-h serum [Na]=(pre-existing ECF [Na]+[Na] added)/(pre-existing ECF+ECF added).

Table 3: **Expected changes after 24 h of fluid administration to an infant weighing 6 kg**

Avoidance of hyponatraemia is essential, but not sufficient, to prevent adverse events associated with iv fluid in all children. Fluid overload occurs in children with impaired free-water clearance who receive 100% or more of maintenance fluid. In a randomised trial of fluid management in bacterial meningitis, facial oedema developed 48 h after admission in 45 of 176 (25·6%) children who received 100% of maintenance fluids using 0·45% saline. The relative risk of death or severe neurological sequelae when facial oedema was present was 2·5 (95% CI 1·4–4·8), despite the absence of differences in serum sodium or osmolarity (Duke T, unpublished). This finding suggests that fluid overload, even without progressive hyponatraemia, can contribute to adverse neurological events, which might be explained by disruptions to the blood-brain barrier in children with meningitis. Thus, generation of cerebral oedema in severe infections is multifactorial: the effective osmolar gradient, administered fluid volume, and a direct effect of antidiuretic hormone on aquaporin proteins are each important.

Table 3 shows the estimated effect of two types of fluid management regimens on serum sodium and volume status in an infant weighing 6 kg, with impaired free-water excretion. Renal function was assumed to be otherwise normal. After use of 0·18% saline at 100 mL/kg per day, serum sodium would be expected to fall from 135 mmol/L to 131 mmol/L within 24 h, associated with a 5% increase in total body water. With 0·9% saline at 75 mL/kg per day, serum sodium would increase by 2 mmol/L and total body water by 1·5%, with no increase in intracellular water. These are the initial changes; secondary effects might include part correction of the fall in serum sodium in those receiving 0·18% saline, because of intracellular water shifts, but increased urinary sodium losses because of expansion of the extracellular fluid.

Few clinical trials have assessed these differences. A non-randomised comparison of 0·18% and 0·9% saline in 24 postoperative patients, showed a similar biochemical effect to our predicted result. Adults receiving 0·18% saline at 3 L per 24 h had a median fall in serum sodium at 24 h and 48 h of 5·4 mmol/L and 7·1 mmol/L, respectively, but serum sodium did not change in those receiving 0·9% saline.[22] In patients in whom renal clearance of free water is reduced by more than 50%, maintenance fluid will need to be considerably less than 75% of normal maintenance volumes to avoid oedema. This approach is not fluid restriction, as it is sometimes interpreted: restriction of fluids to the point of dehydration in the hope of avoiding cerebral oedema is dangerous, and will result in worse outcomes.[23]

Potential pitfalls

Use of an isotonic, rather than hypotonic, solution does not mean that progressive hyponatraemia would not take place, but that it is much less likely. Although use of high-sodium-containing solutions in children with meningitis in the first 24 h was not associated with development of hypernatraemia,[6] during the later phases of illness there is a theoretical risk of hypernatraemia if isotonic saline is used. Diuresis and low urine osmolarity is a feature of the convalescent phase of childhood infections. However, during this phase of illness iv fluid rates are reduced, and enteral feeding reintroduced. Children with severe infections, who are not taking enteral feeds, are at risk of hypoglycaemia; isotonic saline should always have glucose added (5–10%) when given as maintenance fluid. Early correction of clinical signs of severe dehydration or shock is essential.[23]

In renal failure there is no safe substitute for measurement of urine output and serum sodium, and adjustment of water and solute intake accordingly. Severe hyponatraemia should be corrected slowly to avoid the demyelinating syndrome.[23] Although there is no evidence that correction of moderate hyponatraemia in children with isotonic saline causes a large risk of this syndrome, to increase sodium by no more than 1 mmol/L every 2 h, seems sensible when this can be measured. Isotonic saline has a pH of 5–6. When it is used in large volumes for children in shock, metabolic acidosis can persist, and in some circumstances bicarbonate or other buffer might be needed.

Possible solution

We postulate that 0·9% saline (with 5% dextrose) at less than standard maintenance volumes results in a lower frequency of hyponatraemia, seizures, and adverse neurological events than do hypotonic solutions (0·18%–0·3% saline), in acutely unwell children with brain injury of any type (meningitis, encephalitis, cerebral malaria, febrile seizures); serum sodium less than 138 mmol/L;[23] or severe infection associated with greatly impaired free-water excretion.

Ideal testing of this hypothesis would be done in a large randomised controlled trial of hypotonic versus isotonic saline in children with severe infections, stratified for types of infections. However, we think it would be unethical to include some infections, particularly encephalitis and meningitis, because there is already substantial experience of harm from hypotonic solutions and pathophysiological plausibility of the cause of such harm. Such infections also have a much higher risk than do other infections of cerebral oedema and adverse outcomes if hyponatraemia occurs.

An alternative approach, in hospitals in which hypotonic fluids at maintenance volumes are the routine standard of care, would be to change the policy such that isotonic saline at reduced infusion rates (60–70% of maintenance) becomes the standard iv fluid for seriously ill children. Although not as robust as a randomised control trial, this approach might allow for a detailed before-and-after analysis. Outcomes could include differences in the proportions of children who have neurological events associated with progressive falls in serum sodium. Assessment of harm could include differences in frequencies of severe hypernatraemia, or neurological complications associated with rapidly rising serum sodium.

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Intravenous fluids for seriously ill children

Sir—Trevor Duke and Elizabeth Molyneux (Oct 18, p 1320)[1] once again call attention to a serious clinical problem—hospital-induced hyponatraemia. However, their Viewpoint contains errors of fact and recommendations that are counter to established principles of fluid therapy. The article, like another,[2] inappropriately proposes that isotonic saline be used as maintenance therapy. This strategy poses risks of hypernatraemia and other consequences of sodium overload.[3] These proposals mark a tendency to conflate maintenance therapy with rehydration or restoration therapy—two very separate functions of fluid therapy.

Rehydration or restoration therapy is the first priority of fluid therapy. Rapidly infused isotonic saline, resulting in the restoration of extracellular fluid, is essential in the recovery of adults with cholera and infants with diarrhoeal dehydration. Isotonic saline has been used to treat burn shock since the 1960s. The idea is to temporarily overexpand extracellular fluid to restore circulation.[4] Once accomplished, renal regulation of salt and water balance are also restored. The excess extracellular fluid is mobilised and excreted as urine. Isotonic saline given for these purposes is indexed to bodyweight.

Maintenance therapy, introduced in the 1950s, is replacement of physiological insensible and renal water losses by use of hypotonic saline; these losses vary according to metabolic rate, which is readily estimated from bodyweight, but not to bodyweight itself. The average amount required is 100 mL per 100 kcal (419 kJ) per day; adjustment to that average is appropriate when projected losses differ from average.[5]

We have accumulated evidence that children admitted to hospital because of acute illness or scheduled for surgery are often mildly hypovolaemic; concentrations of plasma antidiuretic hormone are increased, inhibiting free water excretion. Administration of maintenance fluids as hypotonic saline in that setting risks hyponatraemia. Rapid expansion of the extracellular fluid of these patients with 20–40 mL/kg isotonic saline before maintenance therapy is started, and limiting of maintenance therapy to that recommended in the original 1957 protocol outlined above[5] greatly reduces this risk (unpublished data).

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Sir—Trevor Duke and Elizabeth Molyneux[1] underscore the critical role of appropriately or inappropriately secreted antidiuretic hormone in the development of hyponatraemia in children with severe infections. They claim that centrally acting antidiuretic hormone contributes to intracellular water accumulation in the brain by increasing water transport across aquaporin-4, the water-channel protein predominantly expressed in the perivascular astrocyte endfoot processes and in subpopulations of ependymal cells. In support of this contention, they refer to our publication[2] about the effects of intraventricular administration of arginine vasopressin and atrial natriuretic peptide on the brain water content and its localisation into the intracellular and extracellular space in rats with experimentally induced hyponatraemia. In fact, the regulation of brain-specific aquaporin-4 is not yet fully explored, but the involvement of antidiuretic hormone in this process is not substantiated by experimental evidence.

Treatment of cultured rat astrocytes with the protein kinase C (PKC) activator phorbol ester has been shown to cause a rapid time-dependent and dose-dependent decrease in expression of aquaporin-4 mRNA.[3] Inhibition of mRNA concentrations was not related to their stability nor to de-novo protein synthesis, indicating that regulation of aquaporin-4 mRNA via PKC activation could be at the transcriptional level. The water-channel activity of aquaporin-4 has also be been shown to be regulated by phorbol-ester-dependent protein phosphorylation via the PKC pathway, as shown by the presence of typical consensus sites for phosphorylation in the aquaporin-4 protein and by the striking reduction of aquaporin-4 protein concentrations by phorbol diesters.[4]

Moreover, in cultured cells with features of renal medullary collecting ducts, aquaporin-4 expression can be downregulated not only by PKC but also by dopamine.[5] Dopaminergic regulation of brain-specific aquaporin-4, therefore, should be considered as a possible mechanism in the control of brain water metabolism.

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Author's reply

Sir—I agree with Malcolm Holliday and colleagues that use of only hypotonic saline as maintenance fluid increases the risk of hyponatraemia. There are several strategies to avoid this outcome, and the most practical might depend on the setting and resources available. Giving normal saline as extracellular fluid expansion followed by 0·18% sodium chloride at volumes that take account of the strikingly reduced free water excretion that occurs in serious infections or after surgery will be safe for many seriously ill children.

Our article was not designed to address the issue of adequate volume resuscitation, which should use isotonic fluid. The alternative approach we suggested to maintenance fluid considered that recommendations often suggest giving too much water (100 mL per kg per day).[1] In many hospitals in developing countries, the fluid management suggested by Holliday (use of two types of intravenous fluid and regular monitoring of serum sodium) is unavailable. Even in developed countries, deciding on the maintenance fluid rate is often difficult and results in overestimation.

I recently cared for an 8-week-old infant with streptococcal meningitis who presented to an outside hospital with poor perfusion and a serum sodium concentration of 137 mmol/L. She was resuscitated with 50 mL/kg 0·9% saline. The infant was alert and interactive, and had a normal neurological examination and normal hydration when transferred to our hospital. She then received 0·18% saline intravenously at 69 mL/kg per h. 9 h later she developed seizures and a dilated right pupil. The serum sodium concentration was 131 mmol/L, and a CT scan showed extensive bilateral cerebral oedema. Although the clinical course of meningitis might have had a role in the child's deterioration, iatrogenic hyponatraemia due to hypotonic fluid administration, despite initial appropriate normal saline bolus resuscitation, is the most likely cause of the extensive cerebral oedema.

We proposed that for children with meningitis, other brain injury, or serious illness associated with reduced free water excretion, administration of reduced volumes of isotonic saline plus dextrose (after adequate volume expansion) might be a practical approach. No empirical strategy will be ideal for all children: in renal failure, cardiac disease, or severe malnutrition, the risk of salt retention and water overload might be greater if isotonic saline is used. Although I think that dangerous levels of hypernatraemia are less likely to occur with the strategy we proposed than are dangerous levels of hyponatraemia if 0·18% saline is used, this hypothesis should be tested. Empirical fluid strategies should be assessed in various acute clinical conditions for their effects on serum sodium, body water (measurable by very accurate serial bodyweight), and urinary sodium excretion.

The reference we cited by Vajda and colleagues[2] supports the statement that antidiuretic hormone can act centrally to increase water permeability of the cerebral vasculature and intracellular brain water, and other research by them[3] suggest that aquaporin-4 receptors mediate increases in intracellular brain water. However, Vajda and colleagues are right to correct us that there is no good evidence of a link between these two processes.

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3 Vajda Z, Pedersen M, Fuchtbauer E-M, et al. Delayed onset of brain edema and mislocalization of aquaporin-4 in dystrophin-null transgenic mice. *Proc Natl Acad Sci USA* 2002; **99**: 13131–36.

Sir—Trevor Duke and Elizabeth Molyneux's article[1] on the fluid management of severely ill children is an important step in the reassessment of the current recommendations for fluid management in critically ill children in tropical settings. However, we believe that three issues deserve further emphasis. First, in many children, iatrogenic hyponatraemia can be averted by avoiding the unnecessary use of intravenous fluids: in most disorders that lead to hospital admission in tropical countries, including respiratory distress, children are able to take fluid orally after initial management. Second, as Duke and Molyneux's title suggests, their recommendations are for "seriously ill children"—a group that includes malnourished children, in whom WHO currently recommends the avoidance of sodium-rich resuscitation fluids, for fear of salt overload and cardiogenic failure. Finally, many seriously ill children also present in hypovolaemic shock and require resuscitation, often with large boluses of isotonic solutions.

The emergency triage assessment and treatment guidelines, developed by WHO for use in developing countries, define shock on the basis of a delayed capillary refill time (dCRT; >3 s), cold hands, and a weak, fast pulse.[2] However, studies in Brazil[3] and Malawi[4] suggest that these criteria are insensitive, since in both studies shock was rarely diagnosed (<0·5%), although the case fatality rate in those defined as shock approached 100%. In our hospital on the coast of Kenya, clinical assessment for shock has been part of our routine admission practice for several years. A review of data from children admitted to our paediatric ward during the past 12 months shows that dCRT was present in 8% (case fatality rate 24%), a temperature gradient in 4% (12%), and a weak pulse volume in 3% (23%; unpublished data). Mortality in children without any of these features was 2·6%, suggesting that these signs are useful in identifying

	Sodium concentration (mmol/L)				Total
	<125	125–135	135–144	≥145	
Number of children	26 (5%)	257 (50%)	212 (42%)	17 (3%)	512 (100%)
Age (median [IQR], months)	28 (8–74)	23 (10–44)	25 (11–52)	19 (7–37)	24 (10–47)
MUAC <12 cm	12 (46%)	54 (21%)	38 (18%)	7 (41%)	111 (22%)
Falciparum-positive	9 (35%)	172 (66%)	111 (52%)	8 (47%)	300 (59%)
Respiratory distress	16 (62%)	74 (29%)	79 (37%)	8 (47%)	177 (35%)
Impaired consciousness	13 (50%)	170 (66%)	143 (68%)	14 (82%)	327 (64%)
Coma	7 (27%)	102 (40%)	89 (42%)	11 (65%)	203 (40%)
CRT ≥3 s	10/26 (39%)	78/236 (33%)	51/185 (28%)	7/16 (44%)	146/463 (32%)
Hypotension*	6/25 (24%)	33/234 (14%)	16/191 (8%)	2/14 (14%)	57/464 (12%)
Seizures before or at admission	7 (27%)	145 (56%)	116 (55%)	9 (53%)	277 (54%)
Inpatient seizures					
Non-malarial	2 (14%)	20 (24%)	21 (24%)	3 (33%)	46 (23%)
Falciparum-positive	3 (33%)	36 (21%)	47 (43%)	4 (56%)	90 (31%)
Mortality	8 (31%)	40 (16%)	46 (22%)	6 (35%)	100 (20%)

MUAC=mid-upper-arm circumference. CRT=capillary refill time. *Systolic blood pressure <70 mm Hg if younger than 1 year and <80 mm Hg if older than 1 year.

Clinical characteristics of all children older than 1 month admitted to high-dependency unit

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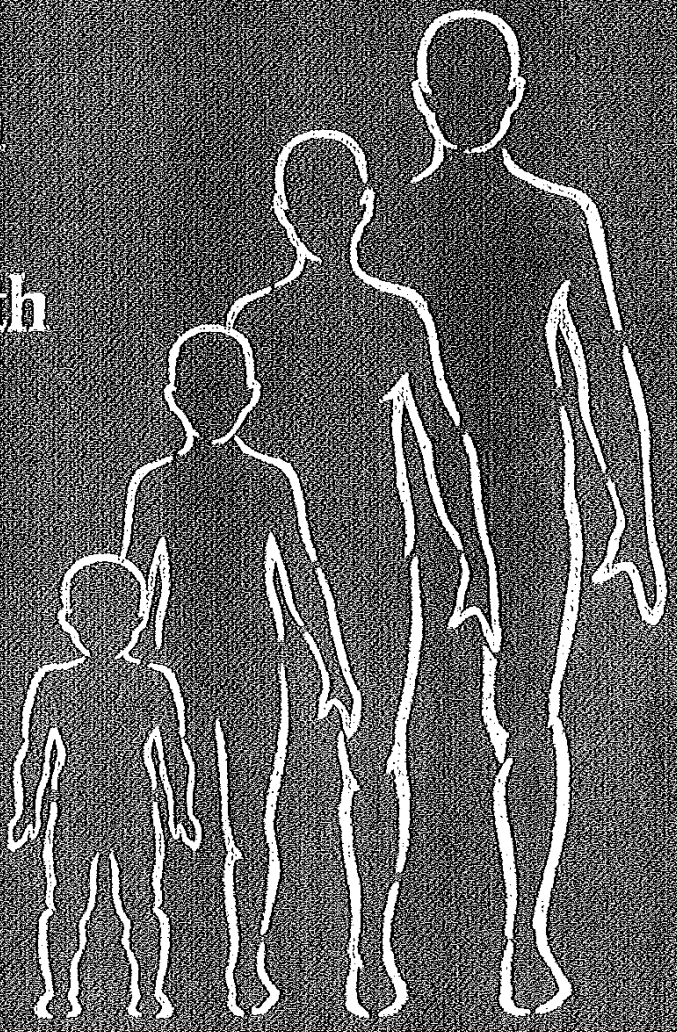

CHURCHILL LIVINGSTONE

sodium and potassium concentrations to the urinary creatinine content (see 'Fractional sodium excretion' below). Further assessment both clinically and biochemically should be made as soon as the response to treatment can be assessed.

The body content and internal distribution of fluid and electrolytes are subject to tight physiological controls and are conveniently interpreted using 'compartment' models. The most important distinction for fluid, electrolyte and acid–base is between the intra- and extracellular environment, which is preserved by the cell membrane. Likewise the composition of the various extracellular fluids depends heavily on the integrity and function of epithelia and the vascular endothelium. The extracellular fluid (ECF) consists of intravascular fluid (plasma) and extravascular fluid. The latter includes 'tissue' or 'interstitial' fluid as well as specialized collections of transcellular fluids formed by secretory activity which include gastrointestinal (GI) secretions, synovial fluid, ocular and cerebrospinal fluids. Body compartments can also be conceptualized if not defined anatomically, by the behavior/ distribution of solutes within them. This latter approach is more commonly applied in pharmacology than physiology but it usefully defines some aspects of the behavior of the body as a compartmentalized vessel. In a 'one-compartment' model the drug, once administered, is assumed to instantly distribute homogeneously throughout the volume of distribution. In a two-compartment model the drug distributes rapidly through a small volume, central compartment that usually corresponds to blood and the extracellular fluid of highly vascular organs and more slowly through a larger compartment, which usually includes adipose tissue and intracellular fluid (ICF).

Both total ECF volume and the distribution of fluid between extracellular compartments can vary widely in disease. Furthermore, one of the main consequences of ECF changes is corresponding or consequential change within the ICF. These changes are dictated by the interplay of hydrostatic, oncotic and osmotic forces, endothelial and cell membrane permeability and the integrity of active homeostatic systems such as membranous Na^+/K^+ ATPase.

DIFFERENCES AMONG BABIES, CHILDREN AND ADULTS

The physiological differences between premature and term neonates and among babies, older children and adults are extreme. From a constitutional perspective, neonates have proportionally the greatest water content and obese adults the least. The 'total body water' accounts for 80% of mass at birth and this percentage falls to 60% by 1 year of age. The change is the result of a disproportionate increase in cell mass (due to growth) compared to the volume of ECF. The percentage of water in postpubertal females is lower than males due largely to their higher percentage of body fat. In both sexes, throughout adulthood, the body water content falls with advancing age.

Children need higher water and electrolyte intakes than adults making them more susceptible to dehydration. Their increased water losses are due to the:

- caloric expenses of a high metabolic rate;
- high insensible loss (high minute ventilation, high surface area:volume ratio, immature epidermis in premature babies);
- decreased ability to concentrate urine.

The distribution of water between the 'compartments' also differs between infants and adults (Table 15.1). During the first few days of life there is a transfer of water from ICF to ECF. This mechanism, which may protect the infant against the effects of dehydration, increases the already large ECF volume and could be a factor in the occurrence of edema sometimes observed at this time. The ICF accounts for an increasing percentage of total body water up to 1 year of age but this is mostly a reflection of the reduction in ECF volume. The ratio of ICF:ECF volume increases from unity, nearing the adult value of 2:1 some time after the age of 1 year.

The sodium content per kilogram body weight is 35–50% higher in the infant than in the adult due to the greater amount of extracellular fluid. With the relative reduction of ECF with growth, adult values are reached at about 2 years of age. Neonatal calcium and phosphate levels are higher than maternal levels, the former as a result of placental function and the latter as a consequence of the resulting fetal parathyroid hormone levels. Intracellular calcium stores are lower however making muscle function (particularly myocardium) more dependent upon the serum ionized calcium.[1] The average plasma concentration of chloride is also higher in babies, like the phosphate levels. Anion/cation balance must exist for there to be electroneutrality and both are balanced by a lower bicarbonate level. Age and gender-related reference ranges should be available from the laboratory for each electrolyte being measured.

As already stated, babies have a higher obligatory urinary water loss than older children and adults, a consequence of a higher urinary solute load and a decreased concentrating ability (to about 600 mosm/L).[2] These features are a consequence of tubular immaturity, one aspect of which is that fewer nephrons have loops which extend into the renal medulla. The result is a much higher flux of water and electrolytes. A term infant exchanges about one-half of his ECF in the day whilst an adult exchanges only one-seventh. Renal immaturity is accentuated in the premature infant.[2] It manifests in a number of ways including a tubular leak of bicarbonate creating a tendency towards metabolic acidosis and an almost unique ability to develop genuine sodium depletion through urinary losses even in the absence of diuretics.

Babies also have a reduced ability to deal with a water load,[2] a consequence of a low glomerular filtration rate (GFR). The GFR subsequently increases over the first 6 months of life.

Table 15.1 Partition of body fluids (average figures)

	Adult (70 kg; 1.85 m²)			Infant (3 kg; 0.2 m²)		
	% Body weight	Liters	Liters/m²	% Body weight	Liters	Liters/m²
Intracellular	40	28	15.2	38	1.14	5.70
Extracellular						
Interstitial*	16	11.2	6.0	33	0.99	4.95
Plasma	4	2.8	1.5	5	0.15	0.75
Total	60	42	22.7	76	2.28	11.4

* Includes transcellular fluids.

MAINTENANCE FLUID AND ELECTROLYTE REQUIREMENTS

The prescription of fluids for children has three components:

1. meeting maintenance requirements;
2. coping with ongoing losses;
3. correcting fluid and electrolyte deficits.

The first two components will be dealt with here. The correction of fluid and electrolyte deficits is covered under 'Fluid and electrolyte disturbances' below.

Normal water requirement is closely linked to energy requirements, both on account of the associated heat production and the urinary solute load resulting from the diet. A normal infant requires 110 cal/kg body weight/day and, it is claimed, approximately 150 ml fluid (i.e. solution) per 100 cal expended. For babies an enteral food source is available which balances calories and volume perfectly. A breast-fed term newborn drinks approximately 150 ml/kg/day. This gives the baby 100 kcal/kg/day of energy (the creamatocrit of breast milk increases during a feed but on average it contains 67 kcal/100 ml or 20 kcal/ounce). This ratio of water to energy promotes optimum growth. However 150 ml of milk does not contain 150 ml of water and the volume requirement of enteral milk (150 ml/kg/day) does not transpose to the prescription of parenteral fluids.

In contrast to fats, carbohydrates and salts have low volumes in solution and when parenteral fluids and nutrition are limited to a few days in a previously healthy child, a calorie intake of 20–35% of the average normal requirement will suffice. Thereafter a more comprehensive approach is required. Catabolism due to illness is unresponsive to hyperalimentation and feeding in excess of metabolic requirements during illness increases morbidity.[3,4] Fluid provision needs to be adapted to the circumstances. Even when water intake is zero during illness, appreciable quantities of water are being produced by the oxidation of the hydrogen content of tissues undergoing catabolism and water is preserved by increased antidiuretic hormone (ADH) levels. Baseline 'maintenance' fluids are a considerable overestimation of water requirement for most hospitalized patients. Indeed unrestricted fluid regimes should only be allowed in enterally fed patients when relying on satiety. Mandatory reductions to baseline fluids apply for patients receiving i.v. fluids, nursed in bed, paralyzed, breathing humidified gases or being nursed in a humidified environment. All fluids administered must be taken into account in the fluid balance including drugs, flushes for i.v. and intra-arterial (i.a.) lines etc. A regime for making interactive decisions about fluid management is summarized in Table 15.2.

For example, using this regime, a 10 kg child being ventilated for bacterial pneumonia might be prescribed an i.v. fluid regime of 100 ml/kg × 0.75 (for breathing humidified gases) × 0.7 (if paralyzed) × 0.7 (for the risk of high ADH levels) = 37 ml/kg/day. Subsequent provision would be judged in the light of fluid balance (weight), plasma urea and electrolytes and urinalysis.

A normal dietary sodium intake ranges between 1 and 4 mmol (23–2 mg)/kg body weight/day. The normal daily dietary potassium intake ranges between 1 and 3 mmol (39–117 mg)/kg body weight. A 500 ml bag of 4% dextrose and 0.18% saline with 10 mmol of potassium added to each bag when infused at 100 ml/kg/day provides; 16 calories/kg/day, 3 mmol/kg/day of sodium and 2 mmol/kg/day of potassium. 10% dextrose infused at the same rate provides 40 calories/kg/day which is 6.9 mg/kg/min of glucose which satisfies the normal immediate calorie requirement for babies.

ONGOING LOSSES

Stipulated 'normal' maintenance requirements include an allowance for natural sensible and insensible losses. To prospectively compensate for abnormal fluid and electrolyte losses, the volumes involved must be measured and recorded and the composition of the fluid determined (Table 15.3). The primary fluid loss is always from the extracellular compartment and its composition can often be anticipated according to its origin. Acute losses from the intravascular compartment can be replaced directly. Furthermore equilibration of fluid and electrolytes occurs between compartments (particularly between the ICFs and ECFs). The ICF is not directly accessible and replacement regimes devised to compensate for previous (as opposed to current) losses are

Table 15.2 Volume of intravenous fluid administered. (From Shann 1999[5] with permission)

		Fluid regime/adjustment
Baseline	1 Day of age	50 ml/kg/day
	2 Days of age	75 ml/kg/day
	3+ Days of age	100 ml/kg/day
	< 10 kg	100 ml/kg/day
	10–20 kg	1000 ml/day + 50 ml/kg/day for every kg > 10 kg
	> 20 kg	1500 ml/day + 20 ml/kg/day for every kg > 20 kg
Decreases	Humidified gases	× 0.75
	Paralyzed	× 0.7
	High ADH (e.g. IPPV or coma)	× 0.7
	Hypothermia	− 12% per °C core temp is < 37
	High ambient humidity	× 0.7
	Renal failure	× 0.3 (+ urine output)
Increases	Full activity and oral feeds	× 1.5/free fluids
	Fever	+ 12% per °C core temp is > 37
	Room temp > 31°C	+ 30% per °C
	Hyperventilation	× 1.2
	Preterm neonate (< 1.5 kg)	× 1.2
	Radiant heater	× 1.5
	Phototherapy	× 1.5
	Burns day 1	+ 4% per 1% of body surface area affected
	Burns day 2 +	+ 2% per 1% of body surface area affected

ADH, antidiuretic hormone; IPPV, intermittent positive pressure ventilation