Case No: HQ12X02550

Neutral Citation Number: [2015] EWHC 51 (QB)
IN THE HIGH COURT OF JUSTICE
QUEEN'S BENCH DIVISION

Royal Courts of Justice
Strand, London, WC2A 2LL

Date: 16/01/2015

Before :

THE HON. MRS JUSTICE SWIFT DBE

- -

Between :

ST (a Protected Party by his mother and Litigation Friend, KT)	**Claimant**
- and -	
Maidstone and Tunbridge Wells NHS Trust	**Defendant**

- -
- -

Mr Andrew Post QC and Miss Jane Tracy-Forster (instructed by **Thomson Snell & Passmore Solicitors**) for the **Claimant**
Mr Angus Moon QC (instructed by **Weightmans LLP**) for the **Defendant**

Hearing dates: 13 – 20 October and 23 October 2014

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Judgment

Mrs Justice Swift DBE :

INTRODUCTION

1. This is a clinical negligence claim by the Claimant, a child and Protected Party, who acts by his mother and Litigation Friend, KT. The claim concerns events which occurred at the Defendant's Pembury Hospital, Tunbridge Wells, during the period between 24 and 27 November 2004, when the Claimant was two and a half years old. He is now aged 12 years.

2. The Claimant suffers from at least one, and probably two, congenital haematological conditions. As a result, he was, from an early age, prone to become anaemic. The level of haemoglobin (Hb) in his blood tended to be low and required careful monitoring. Over the first two and a half years of his life, he required a number of blood transfusions when his Hb level dropped.

3. On the evening of 24 November 2004, the Claimant was unwell and was taken to hospital where blood samples were taken. The ensuing blood tests showed that his Hb level was very low. Nevertheless, he was not given a blood transfusion that night. Instead, transfusion began at 11.20hrs the following day.

4. The Defendant has admitted that, by failing to admit the Claimant to hospital on the evening of 24 November and by delaying performance of the blood transfusion until mid-morning the following day, it was negligent. The Claimant alleges that the Defendant was also negligent in that its medical staff (a) failed promptly to administer intravenous (IV) fluids when the Claimant became dehydrated and (b) gave the Claimant a diuretic drug, Frusemide (now known as "Furosemide"), during the transfusion on 25 November 2004 and also during a second transfusion which was carried out on 26 November 2004. The Defendant denies negligence in those two respects.

5. On 27 November 2004, the Claimant suffered seizures. He was found to have had a series of strokes, as a result of which he suffered brain damage and has been left with severe and permanent disability.

6. I have heard the trial of the issues of breach of duty and causation. The primary issue is that of causation, i.e. whether there was a causal connection between the admitted delay in transfusing the Claimant (together with the other breaches of duty, if proved) and the development of his strokes and consequent brain damage.

7. The trial necessarily focussed primarily on the detailed investigation of a number of very complex medical issues. No one involved in it could forget, however, that the events of November 2004, whatever their cause, were a tragedy for the Claimant and for his family.

THE TRIAL

Representation

8. During the trial hearing, the Claimant was represented by Mr Andrew Post QC and junior counsel, Ms Jane Tracy-Forster. The Defendant was represented by Mr Angus

Moon QC. Counsel displayed a most impressive knowledge of the relevant medical issues and I was greatly assisted by them.

Lay evidence

9. Witness statements from the Claimant's parents, both his grandmothers and a great aunt were admitted in evidence. The witnesses were not called to give oral evidence since the Defendant had indicated it did not wish to cross-examine them. Their evidence related primarily to the Claimant's condition from the time when he became unwell prior to 24 November 2004 until the occurrence of his strokes.

The medical evidence

10. The oral evidence was from seven medical expert witnesses, who came from four areas of expertise.

11. Dr Martin Becker, Consultant Paediatrician, was called by the Defendant. Between 1984 and 2011, he practised at the Hinchingbrooke Hospital, in Huntingdon, Cambridgeshire. He retired in 2011, since when he has continued to act intermittently as a part-time Locum Consultant Paediatrician for the Cambridgeshire Community Services NHS Trust. He has also worked as a Clinical Teacher in Paediatrics and Child Health at Cambridge University. He has considerable experience of working with children in the context of a large District Hospital.

12. Evidence about the computerised tomography (CT) scans and magnetic resonance imaging (MRI) of the Claimant's brain that have been undertaken was given by two Neuroradiologists. Dr 'Kling' Chong gave evidence for the Claimant. He is a Consultant in Paediatric Neuroradiology at Great Ormond Street Hospital for Children, London, and has in the past also worked in Neuroradiology in Toronto and Philadelphia. His area of clinical expertise is the interpretation of MRI and CT scans of the paediatric central nervous system. The Defendant called Dr Wellesley St. Clair Forbes who, until his retirement from NHS practice in May 2009, worked as a Consultant Neuroradiologist at Salford Royal Hospitals NHS Foundation Trust and Manchester University Children's Hospital NHS Trust. In addition, he was a part-time Lecturer in the Department of Diagnostic Radiology at the University of Manchester. He has a particular interest in paediatric neuroradiology.

13. Evidence about the haematological issues was given, for the Claimant, by Dr Paul Telfer. He is an Honorary Consultant in Haematology at St Bartholomew's and the Royal London Hospital NHS Trust Hospital and Senior Lecturer in Haematology at Queen Mary, University of London. He has a specialist interest in inherited red blood cell disorders affecting children and adults, notably the congenital disorders from which the Claimant suffers. He has published widely on such disorders, in particular the congenital blood disorder, sickle cell disease (SCD), and is a member of a number of influential organisations within the field of haematology. The Defendant's witness in this field was Dr Paula Bolton-Maggs. She is a Consultant Haematologist who spent 16 years practising at the Royal Liverpool Children's Hospital, then the Manchester Royal Infirmary. Since October 2011, she has been employed as Medical Director of the UK National Haemovigilance Programme known as "Serious Hazards of Transfusion (SHOT)". SHOT is an independent body which provides data to many NHS bodies. Dr Bolton-Maggs is also an Honorary Senior Lecturer at the University of Manchester. She

has a specialist interest in blood coagulation (clotting) and transfusion and has published very extensively on these subjects. She was lead author on the British Committee for Standards in Haematology Guidelines on the Diagnosis and Management of Hereditary Spherocytosis (HS), which is one of the congenital disorders from which the Claimant suffers.

14. Two Consultants in the field of Paediatric Neurology were also called to give evidence. The Claimant relied on Professor Fenella Kirkham, who has been a Consultant Paediatric Neurologist since 1990. From 1990 until 1999, she was Senior Lecturer in Paediatric Neurology at the Institute of Child Health, with an honorary contract at Great Ormond Street Hospital. She currently works part-time as a Consultant Paediatric Neurologist at Southampton General Hospital and also as a Reader at the University of London Institute of Child Health and the University of Southampton. She has published widely in the field of ischaemic brain damage and stroke in childhood. The Defendant's witness was Dr Finbar O'Callaghan, who is a Reader and Honorary Consultant in Paediatric Neurology based at the Institute of Child Health, with a clinical practice at Great Ormond Street Hospital. He has a research and clinical interest in paediatric cerebrovascular disease, including strokes. Both Professor Kirkham and Dr O'Callaghan are involved in work for the International Paediatric Stroke Study (IPSS).

15. The two Neuroradiologists had a telephone discussion ("the Joint Discussion") in February 2014, at which they addressed an Agenda of Questions agreed by the parties. Their responses to those Questions were detailed in a signed document. The other five medical experts also held discussions (which I shall refer to as "the Joint Meeting") in April 2014 and also recorded in writing their responses to the Agenda of Questions put to them. I have referred to that document as their "Joint Statement".

16. There can be no doubt that the medical experts have a collective wealth of knowledge and experience in what are very complex and specialist areas of medical expertise. It is common ground between them that it is impossible to know for certain precisely what happened to the Claimant's blood vessels between 25 and 27 November 2004. There is no obvious or easy answer. What the experts - in particular the Haematologists and Paediatric Neurologists - have sought to do is to form their own view as to what caused the serious brain damage to the Claimant. In reaching my conclusions as to what was the probable cause, I have had to make decisions as to which evidence I prefer on a range of relevant issues. In doing so, it is inevitable that I have to decide on occasion that the evidence of one expert is more reliable than that of another. I shall make clear when I am doing that as I deal with the various issues later in this judgment. For the present, however, there are a number of observations I should make in relation to some of the witnesses.

17. I found the Claimant's Neuroradiologist, Dr Chong, to be a fair, balanced and impressive witness. At the experts' Joint Discussion, the Defendant's expert, Dr Forbes, had to concede that he had previously misinterpreted the CT and MR imaging and had mistakenly concluded that there was some abnormality of the anterior circulation of the Claimant's brain, whereas in fact the impression of such abnormality had been caused by artefactual issues. Interpreting radiological images must be a very difficult task, particularly where, as here, the imaging quality is not very good. However, the error causes me to be cautious about accepting Dr Forbes' evidence relating to the detail of the abnormalities evident on the radiological imaging.

18. Dr Becker was plainly a very experienced clinician. However, he relied on the 1992 edition (rather than the most recent 2011 edition) of an authoritative Textbook which was of some importance to the case (see paragraphs 59-60 and 70 of this judgment). His Report did not make clear the fact that there had been a failure to administer IV fluids which had been ordered for the Claimant (see paragraph 37). Those and other aspects of his evidence to which I shall refer later in this judgment meant that I was not able to place total reliance on him as a witness.

19. As to the Consultant Haematologists, Dr Telfer's evidence was in some respects unsatisfactory. In particular, he had a change of mind between the experts' Joint Meeting and the trial on the subject of the Claimant's haematocrit levels and the consequent likelihood of his having dehydration sufficient to cause increased blood viscosity: see paragraphs 127-128. Of course, a change of mind by an expert after a Joint Meeting does not necessarily suggest unreliability; it may result from mature reflection or reconsideration of the relevant literature. However, on this occasion, the change appeared to be based on a misunderstanding of the relevant data. On the topic of hypocapnia, Dr Telfer did not comment at the Joint Meeting, saying that he "did not know". In oral evidence, however, he supported Professor Kirkham's views on the topic. Once again, these and other aspects of his evidence, meant that, in relation to some issues, I did not feel able to rely on that evidence. By contrast, I found Dr Bolton-Maggs a measured, straightforward and impressive witness, who plainly has considerable knowledge of HS, the condition from which the Claimant suffers.

20. Moving to the Paediatric Neurologists, Professor Kirkham's evidence appeared to be based very largely on her own clinical experience and her own impressions and beliefs, rather than on objective evidence and epidemiological material. It sometimes appeared to be founded on her experience of SCD, which is a condition very different from the HS from which the Claimant was suffering. Her answers to questions were lengthy and, at times, appeared to stray beyond the point. On a number of occasions, I got the impression that she was struggling to explain an absence of positive evidence in support of a view she held. Her references to medical literature were at times inaccurate, in that the document relied upon did not support the assertion for which she was seeking to use it: see e.g. paragraphs 130 and 164. These aspects had an adverse effect on my assessment of the general reliability of her evidence, particularly when the assertion she was making appeared somewhat speculative.

21. Dr O'Callaghan had a very different style. Both his Report and his replies in oral evidence were concise and addressed to the relevant issues. His approach to the epidemiological material was careful, accurate and well-researched and he was careful also not to step outside his area of expertise. He was criticised by the Claimant's counsel, Mr Post, for not explaining his preferred mechanism for the strokes and its location in greater detail in his Report and at the Joint Meeting. Dr O'Callaghan's response was that he believed that his meaning would have been clear to the other experts reading his Report or taking part in the Joint Meeting; he said that he had not included further detail because he did not regard it as necessary. In cross-examination, he was asked why his answer at the Joint Meeting to the Question, "Was this (i.e. the occlusion of the basilar artery) caused by emboli or focal arteriopathy?", was not "both", rather than merely "focal cerebral arteriopathy". The point being made was that, since he was now saying that the focal cerebral arteriopathy had led to embolisation, he must either have changed his mind or must have been deliberately

choosing not to set out his theory fully in the Joint Statement. He responded that it was an artificial distinction to say that arteriopathy and embolism are mutually exclusive and, so far as he had been concerned, it had been obvious that, if arteriopathy had occurred in the Claimant's case, embolisation must have followed and resulted in his injuries. I found those answers entirely convincing and, indeed, the approach he had taken in his Report was consistent with his manner of giving his oral evidence. The impression I formed was that he was doing his best to give a fair and balanced view. That is not to say that I accept his evidence on every point, but I can see no basis in the criticisms made of him. Nor do I accept, as was suggested by Mr Post, that he was wholly mistaken about the radiological evidence.

THE CLAIMANT'S CONGENITAL CONDITION

22. Early in the Claimant's life, he was found to be severely anaemic. As a result, he received a number of blood transfusions and was referred to King's College Hospital, London (King's) for investigation. At King's, he was under the care of Dr David Rees, Senior Lecturer in Haematology. Eventually, he was diagnosed as suffering from a form of congenital hereditary spherocytosis (HS). HS is one of a wider group of inherited disorders of the blood cells, known as congenital haemolytic anaemia (CHA) and is probably the commonest type of inherited CHA in the North European population. In this condition, a genetic mutation affects one or more of the proteins which maintain the integrity of the red blood cell membrane, causing loss of the membrane and a decrease in the surface area of the red cell. In unusually severe cases of HS, regular blood transfusions are required to maintain an adequate Hb level. In most cases, however, transfusions are needed only during episodes of sudden worsening of the anaemia. Such worsening can often be caused by infection. Anaemia in HS can be improved by splenectomy (removal of the spleen). This is usually done in severe cases and then only after the age of five or six years, when the child is not so susceptible to bacterial infection.

23. The Claimant is also considered to suffer from another type of CHA, namely congenital pyruvate kinase deficiency (PK deficiency). That condition results in deficiency of an enzyme in the red cells of the blood. The combination of HS and PK deficiency in the same individual is very rare.

THE CLAIMANT'S HEALTH UP TO NOVEMBER 2004

24. In his infancy, the Claimant had several episodes of infection. Between the time of his birth on 16 April 2002 and the end of that year, he underwent three blood transfusions when he was found to have a low Hb level. The lowest level recorded in that year was 4.8, on 10 December 2002. Four more transfusions were carried out in 2003. On 22 April 2003, his Hb level was 4.2 and, on 17 August 2003, 4.5. The Hb level for a normal child of two years is 11-11.5.

25. In October 2003, Dr Rees wrote to the Claimant's GP, reporting on his progress. He described the Claimant as "doing well" overall, with height and weight close to the 50th centile. Dr Rees indicated that the current plan was to give the Claimant blood transfusions when he became symptomatic and also if his Hb level fell below the level of 5.

26. The medical records show that, on 2 June 2004, the Claimant's Hb level was 5.7 and he had a non-specific illness. He was transfused. On 7 August 2004, his weight was measured at 13.7 kgs. On that day, he was described as "tired" with a cough and wheeze. His Hb level was 6.2 and he was again transfused.

27. In a further letter to the Claimant's GP, dated 22 November 2004, Dr Rees reported a recent telephone conversation between himself and the Claimant's mother. He indicated that the Claimant's Hb level had been "fairly stable" at 5-6 since June and that he seemed to keep "reasonably well" at that level. He said:

> "His mother knows that should he deteriorate in any way then he should have an urgent blood count and may need a blood transfusion."

He considered it likely that the Claimant would "manage" with his low Hb and the "occasional transfusion" until he was 5 or 6, when a splenectomy was likely to be beneficial.

28. In her witness statement, the Claimant's mother describes how, before November 2004, the Claimant was generally "a normal, happy little boy" who was "walking and talking, and riding a quad bike". The Claimant's father describes how, when the Claimant's Hb levels fell, he would look pale and become jaundiced (i.e. his skin would look yellow). Once he had been transfused, however, he would quickly pick up within an hour or so and be "his old self" again. The statements of the other lay witnesses paint a similar picture.

THE DAYS BEFORE 24 NOVEMBER 2004

29. The lay witnesses describe how the Claimant became unwell a few days before 24 November 2004. His mother describes him as having a cough and cold. His father says that he became tired, lost his appetite and "started to become noticeably jaundiced".

THE PERIOD FROM 24 TO 27 NOVEMBER 2004

24 November

30. On 24 November, the Claimant's mother had intended to take him out for the day. However, he was "really poorly", with noticeable signs of jaundice, tiredness and complaints of pain. He would not eat, although he was drinking. He did not go out and, in the early evening, his mother and grandmother took him to Pembury Hospital. A clinical record, timed at 20.00hrs and written by Dr Gika, Specialist Paediatric Registrar, stated:

> "Cough, cold, lethargy …
>
> Unwell for 1/52 (*i.e. 1 week*) [*with*] cough/cold.
>
> Got more miserable today [*with*] reduced activity although drinking OK. Lethargic since this p.m. Looks more pale and yellow than usually …PU (*passing urine*) …
>
> [*no*] vomiting; [*no*] diarrhoea.

> Temp (*temperature*) 38° (*i.e. above normal level)*
>
> Very quiet but awake and cooperative.
>
> Looks very pale and jaundiced …
>
> Tachycardia (*abnormally rapid heart rate*) (HR 160/min) (*normal rate 70-100)*…
>
> RR (*respiratory rate*) – 24/min
>
> No resp (*respiratory*) distress
>
> Diagnosis ..? viral infection causing deterioration of haemolytic anaemia …
>
> FBC (*i.e. a blood count was to be performed*), cross match …
>
> R/v (*review*) (*with*) FBC result*"*

31. The evidence of the Claimant's mother is that, after examining the Claimant, Dr Gika told her that she could take the Claimant home and that the blood count result would be reported by telephone. She was present at a conversation between Dr Gika and a nurse, in which Dr Gika suggested that the Claimant might be brought back if the Hb result was "really low", but the nurse replied that it was not the practice at Pembury to transfuse after 22.00hrs unless the case involved an emergency such as a road traffic accident. According to the Claimant's mother, Dr Gika pointed out that, if his Hb level was really low, that would be an emergency, but the nurse repeated that the hospital did not transfuse after 22.00hrs.

32. A further clinical note, signed by Dr Resko-Zachera, Paediatric Registrar, and timed at 22.00hrs, recorded:

> "The result of the blood sample … Hb 3.3
>
> I called the Haem Lab – blood for the [*illegible*] has been ordered"

A further untimed note signed by the same doctor reads:

> "I called to mum and informed to come to the ward for the transfusion tomorrow in the morning.
>
> But if she thinks baby's getting worse – she will come as soon as possible."

That Hb level was of course extremely low when compared with the normal limit of 11-11.5 for a child of the Claimant's age. It was significantly lower than any of the Claimant's previous readings.

33. The evidence of the Claimant's parents is that his father attempted to persuade Dr Resko-Zachera that, because the Claimant looked poorly - worse than he usually did

when his Hb level was low - they should take him to the hospital for the transfusion immediately. The doctor refused to agree and told them that they should bring the Claimant into Pembury the following day at 11.00hrs.

25 November

34. The Claimant's mother's evidence was that his condition became worse overnight. She describes how he vomited several times. Early in the morning of 25 November, she contacted her mother, who telephoned Pembury and spoke to a nurse. The nurse told her that the blood for the transfusion would not be ready before 11.00hrs. The Claimant's grandmother told the nurse that the Claimant would be brought into hospital immediately in any event. They arrived there at about 08.00hrs. By that time, the Claimant was, according to his mother, "extremely lethargic" and "not at all well". When asked whether the transfusion could be done immediately, a nurse replied that the blood was not yet ready. Meanwhile, the Claimant was vomiting and "lying quite lifeless" on the bed. He was not interested in drinking, was running a temperature and Paracetamol was prescribed.

35. A nursing assessment form completed at 09.15hrs records the Claimant's colour as "pale", his respirations as "normal", his consciousness as "drowsy", and his behaviour as "calm". He was reported to have "slight" pain, described as "tummy ache". His temperature was 36º and his weight at that time was 14kgs. He was recorded as "apyrexial" (absence of fever) and it was noted he had vomited three times that morning.

36. At 09.30hrs, the blood test results, including the Hb level of 3.3, and a very high bilirubin level at 337 micromol/l, were noted by Dr Gika, who was by then back on duty. The high bilirubin level suggested that the Claimant was very jaundiced. Dr Gika also noted that blood for the transfusion had been ordered and would be ready at approximately 11.30hrs. She undertook a review of the Claimant and recorded:

> "Looks a lot worse this a.m
>
> Sat 0_2 (i.e. *oxygen saturation*): 100%
>
> Tachycardia (HR-150).
>
> Tachypnoeic (*rapid breathing*) (RR-40)
>
> Very quiet but awake and responsive
>
> Dry lips.
>
> Has been vomiting all night according to mum.
>
> Plan: Blood Tx (*Transfusion Service*) called re: getting blood earlier - will be ready at 11.30hrs unless we want it uncrossmatched …
>
> Transfer to HDU (*High Dependency Unit*) and give 0_2. To d/w (*discuss with*) Dr Robards (*a senior colleague*) re: uncrossmatched blood. Otherwise to give fluids"

The meaning of the word "Otherwise" in that note has been a source of argument to which I shall return later.

37. An untimed document recording the IV fluids ordered for and administered to the Claimant during his time at Pembury shows that, on 25 November 2004, an order was given by Dr Gika for him to have 1200mls of IV fluids, with 50mls to be given each hour. That order is crossed out and, unlike every other entry on the page, there is no record of the 'time started' or the person who administered the IV fluids. It seems clear that they were never given.

38. The records make clear that, at 11.20hrs, the transfusion started. It lasted just over an hour with 210mls of blood being given, and a further 65mls at about 12.20hrs. The rate of transfusion was abnormally rapid, the reason being the severity of the Claimant's anaemia. A note timed at 12.00hrs records that 7mgs of Frusemide were given intravenously "half way through" the transfusion. A further note timed at 12.10hrs was made by Dr Gika, who recorded that it was "written retrospectively". It stated that, half way through the transfusion, the Claimant was "looking already a lot better".

39. At 15.30hrs, Dr Gika recorded:

> "A lot better since he's had the Tx (*transfusion*)
>
> Sitting on bed. Drinking OK. Has had 280ml blood".

Her plan was to have another blood count done at 17.00hrs and then make a decision as to whether to perform a second transfusion. A nursing note written in the afternoon/early evening recorded that the Claimant was "feeling brighter this evening, managing to eat small amount", although his temperature was still raised at 38°. The evidence of the Claimant's mother was that he did not recover as well from the transfusion as he usually did. Unusually, he did not want to eat his favourite food. A nursing note recorded that, at 22.30hrs on 25 November, the Claimant's Hb level was 7.4, so that he had not needed another blood transfusion that night.

26 November

40. At 06.30hrs on 26 November, it was recorded that the Claimant had taken a while to settle but appeared to have had a reasonable night's sleep. A further, untimed, note stated:

> "Had been sick twice this morning – no bile or blood. Floppy this morning.
> Yest (*yesterday)* was alert, had eaten and drank well."

Further blood and other tests were to be carried out. By 11.18hrs, the Claimant's Hb level had reduced to 6.1 and his bilirubin level was up at 378. Another note made during the morning of 26 November 2004 (the time illegible) records that the Claimant:

> "remains very sleepy and lethargic.
> Vomited 1 x green bile stained vomit
> Tolerating small amount of fluid
> Observations satisfactory. Very - yellow coloured - in appearance."

41. On the afternoon of 26 November, the Claimant underwent a further blood transfusion. The precise time is not clear, but it seems likely to have been shortly after 13.15hrs. Over a period of approximately four hours, he was given a total of 250mls of blood. The transfusion was, therefore, far less rapid than on the previous occasion. It was noted that 7mgs of Frusemide were given "half way through transfusion". At 17.30hrs, for the first time since his admission at Pembury, he began to receive IV fluids at a rate of 50mls per hour.

42. A clinical note made by Dr Gika, timed at 13.30hrs but stated to have been "written retrospectively" recorded:

> "In view of condition deteriorating again today and abrupt fall of Hb (from 7.4 yesterday evening to 6.1 this a.m.) – blood Tx given again today."

Dr Gika noted that her impression was that there was a "continuing haemolytic crisis". She discussed the position with Dr Robards, who agreed with her. It was decided that Dr Gika would telephone King's and seek the advice of Dr Rees.

43. A note made at 14.00hrs recorded that the Claimant's urine contained "++blood". At 16.00hrs, Dr Gika noted that she had spoken to Dr Rees who was happy with the Claimant's management so far and had made some suggestions for further investigations of his condition. Those investigations were put in train. At 20.00hrs, a clinical note stated that the Claimant continued to be:

> "… very sleepy c/o pain, mainly in his tummy. ? has UTI (*urinary tract infection*). Colour remains very yellow. … Urine very concentrated and drinking only sips so IV fluids ... commenced at 50mls per hour. Observations in normal limits."

27 November

44. A nursing note timed at 06.00hrs on 27 November recorded that the Claimant had had a "fair night", sleeping well until about 02.30hrs, when he awoke complaining of "tummy" pain and was given Paracetamol. After a while, he settled but woke up at 04.30hrs, again complaining of tummy pain. The administration of IV fluids was continuing, although the device for administering the fluids had to be re-sited as a result of which no IV fluids were given for some time.

45. The Claimant was examined at about 10.00hrs by Dr Kisat, Paediatric Cardiological Specialist Registrar, in the course of a ward round. Two notes of the observations on the ward round exist. The first is signed by Dr Gika and the second by Dr Kisat. Dr Gika recorded that urine analysis had showed that the Claimant had "blood++" in his urine. Her impression was that the Claimant appeared to have haemoglobinuria (i.e. abnormally high levels of Hb in the urine). She noted that the Claimant was:

> "Drowsy again this a.m.
> Crying in pain according to mum
> Not eating/drinking
> Not vomiting this a.m."

46. At the time of the ward round, the Claimant was asleep, but easily aroused and irritable and crying when awake. Dr Gika noted the results of the examination of the Claimant's abdomen and chest. She described his chest as "clear" and recorded her impression (or possibly the impression of Dr Kisat, who was in charge of the ward round) that the Claimant was suffering from a "haemolytic crisis, probably due to viral infection." She arranged for further tests, including an abdominal ultrasound, to be performed the following Monday.

47. Dr Kisat's note of the same ward round was made retrospectively and recorded, *inter alia*, that the Claimant was:

> "Sleepy as before but in some pain and c/o pain in left knee & leg since morning."

On assessment, he found the Claimant:

> "Sleepy but arousable & resisting examinations & crying most of the time when examined
>
> - Still pale and jaundiced
> - Normal limb movements
> - Irritable …".

The plan was to continue IV fluids, check the Claimant's blood and administer Phenobarbitone in an attempt to bring his bilirubin levels down.

48. A nursing note recorded the morning's activities:

> "No improvement this morning, continues to be in pain Observations remained stable until 12 midday when mum observed (*the Claimant)* rolling his eyes and slight leg stiffness. Drs. informed ? cerebral irritation …
> Nil by mouth."

49. At about 13.00hrs, Dr Gika saw the Claimant and noted:

> "High pitched cry. Increased tone of lower limbs. Head persistently looking to the left. Eyes also to the left. Pupils dilated, reacting very slowly. Brisk tendon reflexes both legs …
>
> Imp : Encephalopathy ? infection …"

Dr Gika consulted Dr Kisat and made enquiries of King's Liver Unit about the possibility of liver infection. Meanwhile, the Claimant's vital signs were described as "stable throughout" and he was maintaining his airway. He was transferred to the Pembury High Dependency Unit. Staff at Guy's Hospital Retrieval Team were asked for advice and recommended an urgent CT scan of the brain and for the IV fluids to be changed.

50. At about 15.00hrs, the Claimant had two episodes of bradycardia (slow heart rate), with a high-pitched cry and increased muscle tone of the lower limbs. It was decided that a CT scan of the Claimant's brain should be undertaken. Dr Kisat was consulted and directed that the Claimant also needed intubation (administration of fluids by tube). The attempt to arrange for the CT scan to be performed at Pembury proved unsuccessful since the scanner was broken. It was decided to transfer the Claimant to King's for the CT scan and the Guy's Retrieval Team were asked to make the transfer. Meanwhile, the Claimant was sedated and ventilated. At 17.30hrs, it was recorded on the Paediatric Unit Fluid Chart, "Catheter : No urine".

51. At some time in the late afternoon, Dr Kisat spoke to the Claimant's parents. This note records that he:

> "… told them possibility of haemolytic crisis secondary to probably viral infection. This has probably resulted in encephalitis (*inflammation of the brain*)."

52. The Retrieval Team took some time to arrive and eventually collected the Claimant at 19.30hrs. He was taken to King's, where he was treated until 18 January 2005, when he was transferred back to Pembury.

THE ALLEGATIONS OF BREACH OF DUTY

53. The primary allegations of breach of duty relate to the failure on the part of the clinical staff at Pembury to advise the Claimant's parents to bring him back to hospital at 22.00hrs on 24 November, when the Hb results were known, together with the failure to start the transfusion by 02.00hrs on 25 November at the latest. The Defendant admits those breaches and admits also that the transfusion should have started by 02.00hrs and should have been completed no later than 06.00hrs on 25 November. It is agreed that, had the transfusion taken place promptly, it would have been done over a period of four hours, rather than rapidly over one hour as was the case. In fact the transfusion was commenced at 11.20hrs on 25 November. There was therefore a delay of almost 9½ hours in circumstances where the Claimant was suffering from severe anaemia.

54. The Particulars of Claim also alleged, at paragraph 28(c), that:

> "if the Claimant became dehydrated (which would have been avoided by timely transfusions), IV fluids including dextrose and saline should have been administered at the same time as or before the transfusions".

It is now acknowledged that it would not have been appropriate to administer IV fluids <u>during</u> the transfusions. The only complaint is that they were not given before and after each transfusion. In its original Defence, the Defendant alleged that the Claimant had not become dehydrated at all. In its Amended Defence, however, it admitted that he had become dehydrated, but averred that the dehydration was not severe.

55. At paragraph 28(d) of the Particulars of Claim, the Claimant alleged that the clinical staff were also in breach of duty in not giving the Claimant his first transfusion slowly (i.e. over a period of about four hours) and in giving him the diuretic, Frusemide, during

both the transfusions. In its Defence, the Defendant responded that, even if the first transfusion was given too fast, the speed caused no injury. In the event, the allegation relating to speed of transfusion was not pursued. The Defendant also averred that a competent body of practitioners would have given Frusemide at the time of transfusions, and that, in any event, the administration of Frusemide caused no injury.

56. In its Amended Defence, the Defendant also contended that the injuries alleged in the Particulars of Claim (namely the strokes suffered by the Claimant) were not within the scope of the duty of care owed by the Defendant to the Claimant. I shall deal with that issue of law later in this judgment.

THE ISSUES RELATING TO BREACH OF DUTY

57. The issues relating to breach of duty are therefore:

    a) To what extent, if at all, was the Claimant dehydrated between the evening of 24 November and 27 November and, if he was dehydrated, was the Defendant in breach of its duty by not administering IV fluids earlier?

    b) Was it in breach of duty to administer Frusemide during one or both of the transfusions?

    I shall consider these issues separately.

Dehydration

58. Dehydration means a reduction in body water to below normal levels. It upsets the balance of minerals in the body which can affect the way the body functions. Additional adaptive mechanisms come into play, e.g. the kidneys conserve water so that urine is more concentrated and the volume of urine is reduced. When blood plasma volume is reduced as a result of dehydration, the pulse rate increases and blood pressure (BP) decreases. Net loss of water occurs if fluid losses are greater than fluid intake. Fluid losses occur with sweating (e.g. with fever), passing of urine, vomiting and diarrhoea. Dehydration in a child who is ill is not uncommon. It is treated by trying to induce the child to drink more fluids. However, IV fluid replacement may become necessary if oral fluid intake becomes insufficient.

59. In the course of the evidence, I was referred to a passage in the well known publication, *Nelson Textbook of Paediatrics* (19th edition 2011) (*Nelson*). It states:

> "Dehydration, most often due to gastroenteritis, is a common problem in children. Most cases can be managed with oral rehydration. Even children with mild to moderate hyponatremic or hypernatremic dehydration can be managed with oral rehydration."

    Table 54-1 sets out criteria for the clinical evaluation of dehydration:

"**Mild dehydration (<5% in an infant; <3% in an older child or adult)**: Normal or increased pulse; decreased urine output; thirsty; normal physical findings

Moderate dehydration (5-10% in an infant; 3-6% in an older child or adult) Tachycardia; little or no urine output; irritable/lethargic; sunken eyes and fontanel; decreased tears; dry mucous membranes; mild delay in elasticity (skin turgor); delayed capillary refill (>1.5 sec); cool and pale

Severe dehydration (>10% in an infant; >6% in an older child or adult); Peripheral pulses either rapid and weak or absent; decreased blood pressure; no urine output; very sunken eyes and fontanel; no tears; parched mucous membranes; delayed elasticity (poor skin turgor); very delayed capillary refill (>3 sec); cold and mottled; limp, depressed consciousness"

60. The experts agreed that this Table was a useful aid to evaluating the degree of dehydration suffered by a patient. The percentages refer to the proportion of weight loss suffered by the patient as a result of dehydration. *Nelson* continues:

> "The first step in caring for the child with dehydration is to assess the degree of dehydration (Table 54-1), which dictates both the urgency of the situation and the volume of fluid needed for rehydration. The infant with mild dehydration (3-5% of body weight dehydrated) has few clinical signs or symptoms. The infant may be thirsty; the alert parent may notice a decline in urine output. The history is most helpful. The infant with moderate dehydration is evident from an increased heart rate and reduced urine output. This patient needs fairly prompt intervention. The infant with severe dehydration is gravely ill. The decrease in blood pressure indicates that vital organs may be receiving inadequate perfusion. Immediate and aggressive intervention is necessary. If possible, the child with severe dehydration should initially receive intravenous therapy. "

Nelson goes on to give detailed advice as to the management of dehydration, in particular the need for careful monitoring of the patient's fluid intake and output.

61. The experts agreed that there was no evidence that the Claimant was dehydrated on the evening of 24 November. At that stage, he was not reported to have vomited and was said to be "drinking OK". The only possible indicator of dehydration at that time was his high heart rate (160/min), but that may have had other causes.

62. By the following morning, it is clear that the Claimant's condition had deteriorated. His Hb level at that time is not known, but the experts agreed that it is likely to have been lower than on the previous evening, making him even more severely anaemic. He was reported to have been vomiting overnight and had dry lips. The Claimant's Haematologist, Dr Telfer, took the view that he was significantly dehydrated at that

time. In reaching that conclusion, he relied at least partly on his interpretation of the note (timed at 09.30hrs) made by Dr Gika:

> "Plan: Blood Tx called re getting blood earlier. Will be ready at 11.30hrs unless we want it uncrossmatched …
>
> To d/w Dr Robards re: uncrossmatched blood. Otherwise to give fluids."

As I have already said, it is clear that the IV fluids were not administered.

63. Dr Telfer's interpretation was that Dr Gika had intended that, if uncrossmatched blood (which would have been available earlier than crossmatched blood) were not to be requested, then IV fluids should be given pending the arrival of the crossmatched blood at 11.30hrs, i.e. that the matter was urgent because of the signs that the Claimant was becoming dehydrated and IV fluids should not be delayed until 11.30hrs. In the event, it appears that a decision was taken to wait for the crossmatched blood. Despite that decision, the IV fluids were not given.

64. Dr Becker's reading of the note was that Dr Gika had meant that IV fluids should be given only if the blood for the transfusion (whether crossmatched or not) arrived later than 11.30hrs. In his original Report, he had not mentioned the fact that the IV fluids order was never administered. Given the importance of dehydration in this case, that was an unfortunate omission. In oral evidence, he indicated that he assumed that the order for IV fluids had not been administered because the blood became available before 11.30hrs and no IV fluids were therefore necessary.

65. Dr Becker's evidence was that he did not consider that, as at 25 November, there were any indications from which one could draw the conclusion that the Claimant was moderately, as opposed to mildly, dehydrated. In particular, there was no record of sunken eyes, dry mucous membranes, delay in elasticity of the skin or coldness. He did not accept that the "dry lips" referred to in the note made at 09.30hrs would indicate dry mucous membranes; they could, he said, have resulted from a respiratory infection. He attributed the Claimant's increased pulse rate and rapid breathing to his severe anaemia and pointed out that, once he had undergone the transfusion, his pulse rate had reduced. He suggested that the Claimant's reported lethargy, and possible irritability, could be explained by his anaemia.

66. Dr Becker compared the Claimant's weight, as recorded on 24 November (14kgs), with that recorded on 7 August 2004 (13.7kgs). In his original Report, he calculated that, when the Claimant was admitted to Pembury on 24 November, his weight was only 1-2% less than would be expected, applying the percentiles of weight gain that could reasonably be assumed over the period from August to October. In a subsequent letter, written after receiving Dr Telfer's Report, he amended that percentage of expected weight loss to 5-6% and observed that, whilst he accepted that there was a degree of dehydration on 25 November, he classified it as "mild/moderate" and not such as to make it necessary to give IV fluids. He considered that it was reasonable to expect the Claimant to be able to drink, saying that IV fluids replacement were indicated only if a child cannot drink or if there is excessive fluid loss (e.g. as a result of vomiting and/or diarrhoea). A few months later, in an Addendum to his Report, Dr Becker calculated

the Claimant's weight loss at 2.8%. His evidence on this point was, therefore, very inconsistent.

67. It does not seem to me that, on the limited data available, it is possible to assess the Claimant's true weight loss with any accuracy. Only two measurements of his weight were recorded over a three month period and it must, in my view, be possible that the "14kgs" recorded on 25 November was not exact and in fact omitted some decimal points above or below the "14". Dr Becker acknowledged that that might be the case. If the record were not entirely accurate, that would have a significant effect on the calculation of expected weight loss.

68. Some time was spent at trial looking at the records of the Claimant's fluid input and output on 25 and 26 November. However, no detailed fluid charts were kept and, whilst it was possible to gather together some entries contained in the existing nursing and clinical records, it does not appear to me that they can be regarded as complete or as giving an accurate picture of his total input and output of fluids during the relevant period. References to him taking "only sips" and "tolerating small amounts of fluid" do not enable one to calculate his precise intake; the same applies to his urinary output. The failure to keep full and accurate fluid input/output records may have occurred because, as Professor Bolton-Maggs suggested, the staff did not regard dehydration as a key issue at the time, or it may have been an unfortunate oversight. Whatever the cause, it makes the assessment of the true level of the Claimant's dehydration much more difficult. Another feature which causes difficulty is that his serum urea, which Dr Telfer and Dr Becker agreed was the most helpful measure of dehydration, was not tested.

69. Following transfusion on 25 November, the Claimant's condition improved, although not, according to his relatives, to the extent that was usual for him after transfusions. The medical records refer to him "drinking OK" during the afternoon and overnight. His pulse rate had reduced to normal and his Hb, at 7.4, was within normal limits for him, although not for a child without HS. However, he was still vomiting on the morning of 26 November and, by 18.11hrs, his Hb level had reduced to 6.1. The decision was taken to give him another blood transfusion.

70. In assessing whether the Claimant was dehydrated on 26 November, Dr Becker placed some reliance on the urine specific gravity (USG) level of 10.10 as measured from a urine sample taken that day. In his letter of 21 February 2014, he stated that the reading of 10.10 suggested that the Claimant's hydration was at that time within the normal range. In previous editions of *Nelson*, emphasis had been placed on the role of measurement of USG in the assessment of the presence/extent of dehydration. In the most recent, i.e. the 19th, edition (2011), however, the reference to the role of measurement of USG was omitted. From that, I infer that the authors of this authoritative Textbook did not consider that such great reliance should be placed on the USG reading as had previously been thought. Dr Becker (who had referred in his Report only to the 17th (1992) edition of *Nelson*, which included the reference to USG), considered that USG was still a factor to be taken into account. He said that, as a clinician, the Claimant's USG level would have told him that he was not severely dehydrated.

71. Moving to the late afternoon of 26 November, Dr Becker's evidence was that there were still no clinical signs of dehydration and it was clear that the Claimant was able to

take oral fluids. He acknowledged that the records suggested that his fluid input was less than would be appropriate for his body weight, but observed that it was difficult to be certain because of the lack of records. He considered that the Claimant was given IV fluids on 26 November, not because he was believed to have significant dehydration, but for prophylactic reasons, to avoid him becoming dehydrated and because of the difficulty of measuring fluid input and output accurately.

72. The IV infusion continued for the remainder of 26 November and into 27 November, save for two periods when it appears that the device used to administer the IV fluids "tissued" and was removed. By that time, the Claimant was not eating or drinking. By 17.30hrs on 27 November, he had been catheterised and a note recorded, "Catheter – No urine". Dr Becker did not consider that the absence of urine necessarily meant that the Claimant must have been suffering from very severe dehydration. He said that, since the IV fluids had been prescribed for 'maintenance' purposes, one would not have expected a large output of urine. In any event, the Claimant had passed urine only a short time later. He pointed out that, as from mid-afternoon, the IV fluids were reduced to counterbalance the effect of the neuro-complications that were then evident.

73. Dr Telfer believed that the history of vomiting on the night of 24 November and the morning of 25 November meant that the Claimant had lost fluid. He considered that he was moderately dehydrated and that it was because of this that IV fluids were prescribed on the morning of 25 November. He did not consider that his dehydration had been properly managed. His view was that the fact that no urine was found in the bladder after catheterisation on 27 November was significant. It was suggested by the Defendant's counsel, Mr Moon that, in expressing views about the clinical signs of dehydration, Dr Telfer was stepping out of his area of expertise. I do not accept that contention. As part of a team working with Paediatricians on the management of patients, I have no doubt that he has regularly to consider issues such as dehydration, particularly involving children, and is therefore familiar with the clinical and other signs of the condition. He emphasised that dehydration is an important issue. He said that, if the Claimant had been in the care of his team, with severe anaemia, a transfusion to be done, and a history of vomiting overnight and general sickness, he would not have been confident that the child would take sufficient fluids by mouth and would have been likely strongly to advise IV fluids immediately on admission.

74. I do not consider that Dr Becker's interpretation of the note of Dr Gika timed at 09.30hrs on 25 November is correct. It seems to me far more likely that it was intended to mean that, in the event that it was decided <u>not</u> to use uncrossmatched blood (and therefore not to perform the transfusion earlier than about 11.30hrs), IV fluids should be given. Since it was indeed decided not to use uncrossmatched blood, it is difficult to know why the fluids were not in fact administered. It might have been an oversight or a misunderstanding by someone as to what was meant by the note. Alternatively, it might have been a conscious decision made by Dr Gika and/or Dr Robards in the light of the Claimant's condition. If that had been the explanation, however, one would have expected the change of mind to be recorded in the notes. There was no evidence from Dr Gika, Dr Robards or any other witness who might have been able to assist on this point.

75. I consider that, when she wrote the note, Dr Gika must have been aware that the Claimant was showing some signs of dehydration and that, if the transfusion were delayed for a further couple of hours, those signs might well increase. She was well

aware that the transfusion had already been delayed overnight and that the Claimant's condition had deteriorated. I accept that some of the signs of moderate dehydration listed in the *Nelson* Table were not described by the clinicians, the nurses or members of the Claimant's family. Nevertheless, the repeated vomiting, dry lips, tachycardia, lethargy and severe anaemia were, I consider, indicators that the Claimant was probably at the middle-lower end of moderate dehydration (as defined in *Nelson*) at that time. Given the fact that the decision to give IV fluids in certain circumstances was taken and that, despite the fact that those circumstances did in fact arise, they were not administered, I consider that the failure to do so amounted to a breach of duty. There was no evidence of a formal change of plan, nor of the reason for such a change.

76. As to the Claimant's condition thereafter, there was a temporary improvement after the first transfusion, when he was said to be "drinking OK" and his heart and pulse rate had returned to normal. However, thereafter, his condition worsened, he began to vomit again regularly and he was drinking only small amounts. It is most regrettable that his fluid input and output were not better monitored during the period of his admission. That should plainly have been done. As it is, those records which do exist suggest that, during 25 and 26 November and, to a lesser extent, even after IV fluids were started in the late afternoon of 26 November, his fluid input was less than it should have been. The finding at 17.30hrs on 27 November (after 24 hours of IV fluids), that there was no urine in his bladder indicates in my view that, by that time, he was at the high end of moderate dehydration, although his dehydration could not be classified as "severe" within the *Nelson* definition. Indeed, none of the experts suggested that it had been. I consider that, had the transfusion not been delayed as it was, the Claimant would not have become significantly dehydrated overnight on 24/25 November. Thereafter, had the dehydration been adequately managed, with the administration of IV fluids when necessary, it would certainly not have risen to the level it did.

Frusemide

77. The Claimant's case is that the administration of Frusemide, during each of the two transfusions, was in breach of duty. Diuretic drugs act on the kidney to enhance urine production and it is common to administer them during a large volume red cell transfusion, in order to avoid fluid overload. However, Dr Telfer's evidence was that, in the situation of a dehydrated and anaemic child like the Claimant, rapid transfusion of a large volume of blood, together with Frusemide, could be potentially harmful. Dr Telfer said that he would have advised not to give Frusemide unless there was evidence of fluid overload, which there was not in the Claimant's case. It is relevant to note here that an Addendum to the *Guideline on the Administration of Blood Components*, issued by the British Committee for Standards in Haematology, advises that a careful assessment of factors that might give rise to a risk of transfusion-associated circulatory overload should be undertaken before deciding on the volume and rate of a blood transfusion and in deciding whether diuretics should be prescribed.

78. Dr Becker made no reference in his Report to the administration of Frusemide; he had not been asked by the Defendant's solicitors specifically to do so. However, in his letter dated 21 February 2014, written after he had received Dr Telfer's Report, he indicated that he agreed with Dr Telfer that the Claimant had a degree of dehydration and that there was no good reason to give Frusemide during the transfusions. However, in a later Addendum dated 15 September 2014, Dr Becker appeared to change his stance. He gave his opinion that he personally would not have prescribed diuretics in the

Claimant's case, unless he had become concerned during transfusion about the possibility of circulatory overload. He did not consider that it was negligent to give Frusemide to the Claimant at the time of the first transfusion, given that his severe anaemia carried the risk of him developing heart failure and also that it was planned to give the transfusion more rapidly than usual. In oral evidence, he conceded that there was no reason to give Frusemide at the time of the second transfusion, as that was done over a period of four hours, rather than only one.

79. On this issue, I prefer the evidence of Dr Telfer to that of Dr Becker. There is no evidence to suggest that there was a significant risk of fluid overload at the time of the first transfusion or that any assessment of the risk was conducted. The fact that no such assessment was undertaken is to some extent supported by the giving of Frusemide at the time of the second transfusion, when there was not the additional risk factor that the transfusion was to be given rapidly. It appears that it may have been the practice at Pembury to give a diuretic during transfusion. However, given the fact that Frusemide would tend to increase dehydration and that the administration of IV fluids had been planned earlier but not executed, I consider that any competent practitioner would have concluded that to administer Frusemide at the time of both the first and the second transfusion would not be good medical practice. I therefore find that the giving of Frusemide on both occasions constituted a breach of duty.

80. There is no evidence that, taken on its own, the giving of Frusemide would have had a direct effect on the Claimant. The experts were agreed that there was insufficient scientific literature to determine whether its use during the transfusions would have contributed to increased viscosity of the blood. However, it would have made some contribution to the dehydration from which I have found the Claimant was already suffering.

THE PARTIES' CASES ON CAUSATION

The pleaded cases

81. The Claimant's case on causation was set out in paragraphs 29 and 30 of the Particulars of Claim which stated:

> "The Claimant's haemolytic crisis resulted in hypoxia and concurrent hypocapnia and consequently to dehydration due to vomiting and reduced fluid oral intake. If he had been transfused by 06.00 on 25 November 2004 without diuresis, his anaemia would have been corrected before his compensatory mechanisms for maintaining oxygenation reached their limits. He would have recovered sufficiently to maintain a reasonable oral fluid intake and would not have suffered vomiting and consequent dehydration, the latter being exaggerated by the use of Frusemide.
>
> The hypoxia, hypocapnia and consequent dehydration were, on the balance of probabilities the cause of endothelial dysfunction and thus of the formation of thrombus in the heart or in the cerebral arteries or systemic veins with paradoxical embolism into the cerebral arteries. This thrombus produced multiple

> embolisations to the basilar artery and its distribution. These caused multiple strokes in the posterior circulation (as demonstrated on the CT scan). ”

82. By way of clarification, I should explain that an “endothelial dysfunction” is a systemic pathological state of the endothelium, i.e. the thin layer of cells that lines the interior surface of blood vessels. Such dysfunction can give rise to the development of thrombus. A “thrombus” is a clot in the cardiovascular system formed from constituents of the blood. As it passes through the blood system, a thrombus may decrease blood flow in a vessel; it may completely cut off (occlude or obstruct) the vessel, resulting in “thrombosis”. The thrombus may be attracted to the vessel or heart wall without occluding the lumen (inside space) or it may occlude the lumen. A thrombus may result in emboli passing through the system. An “embolus” is a transported mass (solid, liquid, or gaseous) carried through the circulation, which may cause the occlusion of a vessel. If an embolus or emboli cause complete blockage of the blood flow, such occlusion is known as an “embolism”. A “paradoxical embolism” is an embolism of a thrombus of venous origin through a lateral opening in the heart. “Stroke” occurs when the supply of blood to the brain is interrupted or completely cut off, often as a result of thrombus and/or emboli.

83. In its Defence, the Defendant denied the cause asserted by the Claimant and instead alleged at paragraph 18 that:

> “The strokes from which the Claimant suffered were the result of the viral infection from which the Claimant had been suffering. The viral infection caused both a transient cerebral arteriopathy and a haemolytic crisis. The cerebral arteriopathy was the most likely underlying cause of the Claimant’s multiple strokes. The Claimant’s anaemia was not the cause of his strokes. On 24 November 2004 the Claimant had a one week history of cough, cold and lethargy, symptoms suggestive of an ongoing upper respiratory tract infection. The Claimant developed arteriopathy secondary to preceding infection and had multiple strokes secondary to that arteriopathy.

An “arteriopathy” is a disease of an artery; a “cerebral arteriopathy” is an arteriopathy which occurs in the cerebral circulation. When the arteriopathy occurs in a specific area, it is termed “focal”. “Arteriopathy” is one of a number of conditions which falls within the wider term of “vasculopathy”, i.e. a disorder of blood vessels.

84. In response to the Defendant’s contentions on causation, at paragraph 32 of the Amended Particulars of Claim, the Claimant stated:

> “In the event of a finding at trial that focal arteriopathy was the primary cause of perturbation of the blood vessel wall, the Claimant will assert that the following factors caused or made a material contribution to the occlusion of the artery and the consequent ischaemic neurological injury:
>
> a) dehydration;

b) acute-on-chronic haemolysis;

c) severe anaemia;

d) the use of diuretics."

85. At paragraph 19(ii) of its Amended Defence, the Defendant responded:

> "The Claimant's injuries were indeed caused by a focal cerebral arteriopathy secondary to viral infection. If this was the causative mechanism whereby the Claimant sustained his injuries (as the Defendant contends and the Claimant implicitly accepts as a possibility by the proposed amendment to paragraph 32 of the Particulars of Claim) the factors identified in paragraph 32 of the Particulars of Claim made no material contribution to the occlusion of the artery or the consequent ischaemic neurological injury. "

Explanation of the Claimant's case

86. The Claimant's primary case at trial was therefore that, as a result of the breaches of duty, the severe anaemia and haemolysis from which the Claimant was suffering on 24 November worsened and led also to the development of hypoxia/hypoxaemia, hypocapnia and dehydration. The Claimant relied on criteria set out in the well known *Virchoff's Triad*, which identifies the three types of "perturbation", i.e. disturbance which can combine to cause a thrombus. These are (i) perturbation of the blood itself; (ii) perturbation of the blood vessel wall, which can occur as a result of direct vessel trauma or damage to the endothelium; and/or (iii) perturbation of blood flow which, if it becomes sluggish, can lead to the formation of a thrombus.

87. The Claimant's case was that the effect of the hypoxia/hypoxaemia, hypocapnia and dehydration said to have been suffered by him as a result of the Defendant's breaches of duty was to cause the types of perturbation identified in the *Triad* to occur, and to trigger endothelial dysfunction, which in turn caused the formation of thrombus with multiple emboli which went through the blood system, causing occlusion of the basilar artery, multiple infarcts (tissue death due to lack of O_2) and damage to the brain, most particularly to the brainstem which is likely to have caused the severe brain damage from which the Claimant suffers. In particular, it was said that hypoxia and hypocapnia would have had the effect of reducing the O_2 level in the Claimant's blood and decreasing blood flow, whilst dehydration would have rendered the blood more viscous (i.e. thick) and would also have reduced flow.

88. Before considering the evidence relating to those conditions, it is necessary to examine the neuroradiological imaging.

THE NEURORADIOLOGICAL IMAGING

89. There are no images of the Claimant's brain available from the period before his strokes occurred. The only information available to the Neuroradiologists, therefore, consisted of the imaging from a CT scan and an MRI scan performed at King's on 28 November

2004. The CT scan was done at about 00.30hrs, shortly after the Claimant's transfer from Pembury. The MRI scan was performed about 13 hours later, at about 13.50hrs. There was also an MRI scan performed at King's on 22 April 2005.

90. The evidence of the Neuroradiologists related primarily to the area known as the vertebro-basilar territory (also known as the posterior circulation) which supplies blood to the posterior part of the area known as the Circle of Willis and from there to the brain. The two vertebral arteries branch upwards from the subclavian arteries and merge to form the single basilar artery. The basilar artery provides the main blood supply to the brainstem. The two posterior cerebral arteries rise from the basilar artery and supply oxygenated blood to the posterior aspect of the brain (the occipital lobe).

The brain imaging on 28 November 2004

91. There was a good deal of agreement between the two Neuroradiological experts. They agreed that the CT scan showed a focal abnormality in the arterial territory of the left posterior cerebral artery with a more subtle abnormality in the adjacent right parietal lobe. They considered that these abnormalities were consistent with ischaemic infarcts (strokes caused by blockages in the blood vessels in the brain) in the vertebro-basilar circulation. They noted that, at the time of the CT scan, the distal (upper) part of the basilar artery seemed to be flowing normally.

92. The Neuroradiologists agreed that the MRI scan confirmed the abnormalities visible on the CT scan. There were many lesions within the vertebro-basilar territory, suggesting that there were several separate blockages in the smaller cerebral vessels branching from this area. Both experts referred in their Reports to some focal signal abnormality in the upper pons, i.e. within the brainstem. The experts agreed that the MRI scan showed poor blood flow through the basilar artery and reduced flow in the left vertebral and left posterior cerebral arteries. However, they noted that the image quality of the basilar, vertebral and left posterior cerebral arteries was limited.

On 22 April 2005

93. The Claimant underwent further MR imaging at King's five months later, on 22 April 2005. By this time, some of the previously noted abnormalities had matured to show a pattern of atrophy. Others had resolved either completely or partially. The images showed areas of established infarction in the left cerebellar hemispheres and in the right and left occipital lobes, being more extensive on the left. Dr Chong noted that there was a mature lesion in the upper pons of the brainstem, more conspicuous than in the previous images. He also described a "notable restoration of blood flow" in the left vertebral artery and most of the basilar artery, although there was a persisting minor abnormality of flow in the upper basilar artery. Dr Forbes observed that the 2005 MRI scan was of better quality than the earlier MRI scan, as a result of which the basilar artery was now visible. His interpretation of the images was that there were irregularities at the distal end of the basilar artery and in the left posterior cerebral artery which, in his view, were consistent with a vasculopathy.

94. The neuroradiological evidence was consistent with the effects of thrombus which had embolised in the vertebro-basilar circulation, causing occlusion (including occlusion to the basilar artery), ischaemic infarction and brain damage. I shall discuss other aspects of the neuroradiological evidence later in this judgment.

The conditions from which it is said that the Claimant had been suffering prior to his strokes

95. The Claimant's case was based on what were said to be the effects of his severe anaemia, acute-on-chronic haemolysis, hypoxia/hypoxaemia, hypocapnia and dehydration. It is necessary to examine separately the evidence relating to each of those conditions and their possible causative effects.

Severe anaemia and acute-on-chronic haemolysis

96. The Claimant's congenital condition caused him to suffer from time to time from anaemia. Prior to 24 November 2004, he had had periodic admissions to hospital with anaemia. However, his Hb level on 24 November (3.3) was significantly lower than it had been on any previous occasion. There is no doubt that, at the time of his admission to hospital on 25 November, the Claimant was severely anaemic. As the experts agreed, in all probability he was more anaemic than he had been about 12 hours previously.

97. Chronic severe anaemia can be associated with intravascular haemolysis, i.e. a breakdown of red blood cells within the circulation. Acute-on-chronic haemolysis occurs when a patient has chronic haemolysis (as in the Claimant's congenital condition, HS) and then has an acute exacerbation. Such an exacerbation can often be caused by infection which can have the effect of increasing the rate of haemolysis and/or reducing the bone marrow output of red cells. The Claimant had been suffering from an infection for a week before his admission to Pembury in November 2004 and it was accepted by the experts that, on 25 November, he was suffering from acute-on-chronic haemolysis. In the experts' Joint Statement, it was agreed that the severity of his anaemia and of his haemolysis could have been prevented by earlier transfusion, proper management of his dehydration and avoidance of the use of Frusemide.

98. At their Joint Meeting, the experts discussed the effects of anaemia generally and, in particular, the possible effects of the increased level of anaemia caused by the delay in transfusion. They agreed that there is no medical literature suggesting that severe anaemia and/or acute-on-chronic haemolysis caused by HS is a risk factor for thrombus and emboli. Nevertheless, Professor Kirkham's view was that that was the case. Dr O'Callaghan and Dr Bolton-Maggs disagreed. They pointed out that patients with HS have protective mechanisms which mean that they have lower cholesterol and Hb levels and higher bilirubin levels than normal, making them less likely to suffer thrombus and emboli than a patient without HS.

99. Professor Kirkham and Dr O'Callaghan agreed that there is medical literature suggesting that <u>some</u> forms of anaemia, in particular SCD and iron deficiency, may have a causative role in stroke. The condition of SCD is, however, very different from HS; in a patient with SCD, the blood clots more easily than in normal patients and the protective mechanisms present in patients with HS do not exist. As a result, the risk of a patient with SCD suffering a stroke is 200 times greater than that of a normal member of the population. Dr Bolton-Maggs observed that, whilst anaemia suffered by children with severe iron deficiency is known to be linked with stroke, this is not the case with HS.

100. At their Joint Meeting, the experts agreed that, on 26 November, when blood was found in his urine, the Claimant was probably suffering from haemoglobinuria. This suggested

that his haemolysis was intravascular, and was not just affecting the spleen. Since involvement of the spleen is the usual pattern in an HS patient, the experts agreed that it suggested that an additional factor, other than the anaemia, was contributing to his haemolysis. A number of possible alternative factors were suggested; the only one which might possibly apply to the Claimant was infection. The experts stated in their Joint Statement agreed that:

> "Increased intravascular haemolysis in the context of infection could have been a factor although this is speculative as the data are mainly laboratory-based."

101. In his Report. Dr Telfer explained that, although chronic severe anaemia with intravascular haemolysis had been recorded as predisposing children to cerebrovascular damage, this has only been commonly reported in children with SCD. But, in a letter written after the Joint Meeting, he appeared to change his view. He wrote:

> "I think there is a plausible mechanism whereby severe anaemia and intravascular haemolysis may have caused damage to the endothelium and hence prompted thrombus formation."

He pointed out that the Claimant's case was unusual for a patient with HS and said that he considered it likely that a pro-thrombotic state may arise, even though such an event was not recognised in the literature. A pro-thrombotic state is a condition which makes it more likely that a thrombus (and, therefore, embolism and stroke) will arise.

102. Dr Bolton-Maggs did not consider that haemolysis, even intravascular haemolysis, was a factor which would cause thrombosis or embolism unless the haemolysis was "massive". She pointed out that, although HS is not an uncommon disease and frequently gives rise to chronic haemolysis which can often be rendered acute by infection, increased haemolysis in such circumstances has never been reported to give rise to thrombotic events. She dismissed Dr Telfer's theory as "speculative".

Conclusions in relation to severe anaemia and acute-on-chronic haemolysis

103. Whilst severe anaemia and acute-on-chronic haemolysis give rise to certain risks, I have not been shown any convincing evidence that, in general, they give rise to the risk of thrombus or emboli in the case of a patient with HS. Patients with SCD are plainly in a very different category and, although there is also a known risk in cases of iron deficiency, it was not suggested that there were any features of that condition similar to those in HS. In particular, there are not the protective mechanisms which HS patients have. There are many patients who suffer from anaemia and acute-on-chronic haemolysis. If either or both of those conditions were liable to give rise to the risk of thrombus, emboli or stroke, it would be surprising if the fact had not been documented in the medical literature.

104. Dr Telfer's view related solely to a suggested mechanism which he thought was "plausible" and which, in his view, "may have" promoted thrombus formation. I agree with Dr Bolton-Maggs that his view appears somewhat speculative. He certainly did not express it in his Report or at the experts' Joint Meeting. So far as Professor Kirkham is concerned, I have already mentioned my reservations about relying on her evidence

where it is unsupported by the literature. On this point, I felt that she was heavily influenced by her experience of SCD in which the risk of thrombus, emboli and stroke is much higher.

Hypoxia/hypoxaemia and hypocapnia

105. The issues of whether the Claimant was suffering from hypoxia/hypoxaemia and/or hypocapnia and, if so, the effects of those condition(s), are related, so it is convenient to deal with them together.

106. Hypoxia occurs when the tissues of the body (including blood) lack O_2. Hypoxaemia indicates oxygen deficiency in arterial blood. In her original Report, Professor Kirkham referred to the Claimant as suffering from hypoxia (and, by inference, hypoxaemia), although she did not cite any clinical or laboratory evidence in support of her assertion that he was hypoxic. There was no specific discussion in the experts' Joint Statement about the existence of any evidence that the Claimant had been suffering from hypoxia. However, Dr O'Callaghan did state his view that there was no such evidence.

107. Professor Kirkham and Dr O'Callaghan agreed that the 'gold standard' for assessing the presence of hypoxia/hypoxaemia in a patient is to measure his/her blood gas (PO_2) levels. The Claimant's PO_2 level was measured only once during his admission at Pembury, on the morning of 25 November. That measurement was within normal limits. Professor Kirkham accepted that the reading was normal but did not consider that it excluded the possibility that the Claimant was hypoxic.

108. Another, less accurate, means of identifying hypoxia/hypoxaemia is by measuring O_2 saturation in the blood. The Claimant's O_2 saturation was measured with reasonable frequency during his admission at Pembury. The relevant records show the following:

"25 November

09.00hrs	100%	
10.00hrs	99%	
11.30hrs	100%	(receiving O_2 during transfusion)
12.30hrs	99%	
16.00hrs	95%	
18.00hrs	96%	

26 November

06.00hrs	97%	
09.00hrs	99%	
13.10hrs	99%	
13.20hrs	98%	
13.35hrs	100%	(not entirely clear)
14.00hrs	98%	
18.00hrs	99%	
21.00hrs	99%	

27 November

02.00hrs	uncertain (could be 90%; observation "Cool to Touch")
Untimed	95%
10.00hrs	97%
12.00hrs	98%

109. The experts did not agree as to the percentage of O_2 saturation which is normal for a child. Dr O'Callaghan said that the normal limits are usually considered to be between 92% and 100%. Dr Telfer put the limits at between 94% and 100%. Professor Kirkham disagreed with both of them. Her view was that there are no reliable normal daytime limits for O_2 saturation levels. She suggested that, even if O_2 saturation level in a child was as high as 97%, most doctors would be concerned. She said that the test has on occasion been shown to be unreliable and suggested that the measurements were of little value. She considered that, whatever they showed, the Claimant was in a "hypoxic situation" as a result of the severity of his anaemia, caused by the delay in transfusing.

110. Dr O'Callaghan did not consider that there was any evidence that the Claimant had been hypoxic. He relied on the normal result of the Claimant's blood gas test on 25 November. So far as the Claimant's O_2 saturation levels were concerned, he considered that, with one possible exception, they were all within normal limits. That exception (at 02.00hrs on 27 November) was difficult to decipher but might have been 90%, in which case it might have indicated the presence of hypoxia/hypoxaemia. However, the three results after that time were again all within what he regarded as normal limits.

111. Hypoxia gives rise to an increase in lactic acid in the blood (acidosis). Another indicator for the presence of hypoxia/hypoxaemia is the patient's pH level. The pH levels measured on 25, 26 and 27 November were all within the normal limits (7.35-7.45 for a child of the Claimant's age) and therefore did not suggest the presence of acidosis. Indeed, on 25 November, the pH level of 7.508 was in excess of the normal rate and, if anything, was alkalotic, not acidotic. The opinion of Dr Becker and Dr O'Callaghan was that, given these findings, there was no basis for reaching the view that the Claimant had suffered from hypoxia or hypoxaemia. Professor Kirkham disagreed.

112. In the experts' Joint Statement, Professor Kirkham pointed out that, on the morning of 25 November, despite the fact that the Claimant was maintaining his O_2 saturation at 100% and his PO_2 at a normal level, he had low carbon dioxide (CO_2) tension in the blood, i.e. he was suffering from hypocapnia. In their Joint Statement, the experts agreed that the Claimant's levels of CO_2 were consistently low between the morning of 25 November and the late afternoon of 27 November, meaning that he was hypocapnic.

113. Professor Kirkham and Dr O'Callaghan agreed that the Claimant's hypocapnia was probably attributable to the fact that he had been hyperventilating. Dr O'Callaghan considered that the hyperventilation had resulted partially from the Claimant's severe anaemia which had caused him to breathe rapidly in order to increase his uptake of O_2. However, he expressed the view that other factors had also probably contributed to the hyperventilation, one factor being the URTI from which the Claimant was suffering and also possibly some degree of anxiety and pain. He considered that it was likely that, even had the transfusion not been delayed, a degree of hypocapnia would have occurred because of the Claimant's anaemia and viral infection.

114. Professor Kirkham accepted that hyperventilation can plausibly be related to viral illness but considered that most Paediatricians would say that the illness would have to compromise the chest significantly (e.g. as in pneumonia or asthma) for a significant level of hyperventilation to occur. She did not believe that the Claimant's infection was sufficiently serious to cause him to hyperventilate. Nor did she consider that there was any evidence that the Claimant had been anxious at the relevant time. She considered that the hypocapnia was due solely to compensatory hyperventilation, i.e. hyperventilating in order to maintain his pO_2 saturation level. This, she said, would have the effect of reducing his CO_2 tension.

115. Professor Kirkham explained how she believed that the Claimant's body had been compensating for its "hypoxic situation" by hyperventilating. She drew an analogy with mountaineers at high altitudes who may be exposed to a decrease in O_2 to which they react by hyperventilating, and pointed out the incidence of hypoxia and strokes in such cases. She expressed her view that, if the transfusion had been performed when it should have been, that would have corrected the Claimant's anaemia before he "reached the edge" of his compensatory mechanism of oxygenation. In oral evidence, she explained her conclusion thus:

> "Was he hypoxic or not?
>
> - Yes, he had a compensated hypoxia. Anaemia causes hypoxia which is compensated by hyperventilation.
>
> I suggest you are redefining [*the*] meaning of hypoxia – that it exists without acidosis?
>
> - No, this is a hypoxic environment, he is anaemic and he is compensating with hyperventilation to maintain sats."

116. Dr O'Callaghan did not accept that the Claimant had "reached the edge" of his compensatory mechanism for oxygenation on 25 November. He said that "compensated hypoxia" is not a term he recognises as being in normal use. He suggested that it was difficult to see how one could say that the Claimant was "on the verge" of hypoxia/hypoxaemia when there was no objective evidence that his blood gases were falling.

117. Dr Telfer agreed with Professor Kirkham that he did not consider that the O_2 saturation levels provided a reliable picture of whether the Claimant was in fact hypoxic/hypoxaemic. He took the view that the Claimant's low Hb had caused him to be at the very limit of his ability to maintain O_2 in his tissues. He suggested that, since the Claimant's Hb levels were low, the amount of O_2 in the blood was bound to be reduced.

118. The Paediatric Neurologists agreed that hypocapnia can cause vasoconstriction (narrowing of the blood vessels) and slower blood flow. Professor Kirkham's evidence was that hypocapnia therefore "favours" the propagation of thrombus. Dr Telfer had not mentioned hypocapnia in his Report and had declined to comment on it in the Joint Meeting. In oral evidence, however, he said that he considered that hypocapnia could

have an adverse effect on blood flow. Dr O'Callaghan did not accept that hypocapnia necessarily gives rise to an increased risk of thrombus formation. He said that a child with low CO_2 levels may get some narrowing of vessels in the cerebral circulation, but will also get dilation of the pulmonary vessels. On 25 November, the Claimant had an increased heart rate (at 150 beats per min) which would, he said, have increased cerebral blood flow and blood velocity, and would thereby have compensated for the effects of hypocapnia.

119. Professor Kirkham did not agree. Her contention was that the blood flow to the brain was auto-regulated so that, even if the heart rate was increased, the blood flow to the brain would not change. The effect of increased heart rate would, she said, be different to the CO_2 effect, so that cardiac output and heart rate was unlikely to affect cerebral blood flow. Dr O'Callaghan's response to that was that, since the whole aim of auto-regulation is to maintain as much blood flow as possible, it was most unlikely that the body would auto-regulate so as to reduce the blood flow to the brain if vasoconstriction occurred.

Conclusions on hypoxia/hypoxaemia and hypocapnia

120. There is no positive evidence (save, possibly, for the O_2 saturation reading at 02.00hrs on 27 November) that the Claimant had hypoxia or hypoxaemia at any stage prior to his strokes. As to that reading, I am by no means certain that it was "90%". It could equally well have been "95%" or "98%", both of which would have been far more consistent with every other O_2 saturation result during his time at Pembury. In any event, leaving that reading aside, the evidence appears to suggest that the Claimant was probably <u>not</u> suffering from hypoxia or hypoxaemia. The test accepted by both the Paediatric Neurologists as the "gold standard" indicated that he was not. Furthermore, although the O_2 saturation test is plainly not considered to be as accurate, the results did provide some support for the suggestion that he was not hypoxic.

121. Professor Kirkham's explanation of the Claimant's "hypoxic situation" and its effects, which was to some extent supported by Dr Telfer, <u>may</u> be correct, but I did not find it wholly convincing. There was no reference to it in Professor Kirkham's Report or the Joint Statement, merely a bold assertion in her Report of the fact that the Claimant was suffering from hypoxia. Furthermore, the mechanism explained by Professor Kirkham was not supported by any authoritative literature. She did produce a Paper dealing with the effects of stroke at high altitude but, since it concerned adults aged between 22 and 48 years who had had a long term stay at high altitude - a situation rather different from that of the Claimant in November 2004 - I did not find it very helpful. I preferred the evidence of Dr O'Callaghan, which was based wholly on the available test results and on the conventional meaning of the term "hypoxia". I do not consider, on a balance of probabilities, that the Claimant was at any stage suffering from hypoxia or hypoxaemia.

122. There is no doubt, however, that the Claimant was hypocapnic throughout his time at Pembury and that this was because he was hyperventilating. It is accepted that one cause for his hyperventilating was his severe anaemia which was likely to have been made worse by the delay in carrying out his transfusion on 24 November. However, I do not accept Professor Kirkham's evidence that the Claimant's hyperventilation was caused solely by the effects of his "hypoxic situation". I regard it as probable that, as Dr O'Callaghan suggested, the URTI from which he was suffering made a contribution to his hyperventilation and therefore to his hypocapnia. I have no doubt also that, given

the Claimant's age and the fact that he was very unwell and in hospital, he must have been suffering from a degree of anxiety which contributed to his hyperventilation. On the morning of 25 November, he was also complaining of a degree of pain, "tummy ache". Whether Dr O'Callaghan is correct that the Claimant would not have avoided hypocapnia even had the delay in transfusing not occurred, I am not sure. However, it seems to me that his infection, anxiety and discomfort must have played a significant part in his hyperventilation on the morning of 25 November and thereafter.

123. As to the effects of his hypocapnia, I prefer the evidence of Dr O'Callaghan to that of Professor Kirkham. Whilst it is the case that hypocapnia is known to be capable of causing vasoconstriction and slower blood flow, I found Dr O'Callaghan's explanation of how the protective mechanisms in HS patients can guard against the formation of thrombus and emboli wholly convincing. Professor Kirkham's explanation of how the protection was unlikely to have any effect was somewhat surprising. Dr O'Callaghan's response to the effect that her explanation was inconsistent with the principle of the body's auto-regulation mechanisms seemed to me to make far more sense. I note also the absence of any medical literature showing that hypocapnia or hyperventilation following severe anaemia and acute-on-chronic haemolysis is known to be a cause of thrombus, emboli or stroke in a child suffering from HS.

124. In short, I can find no convincing evidence that the effect of hypocapnia for a child in the Claimant's position was to cause vasoconstriction and/or slow blood flow such as to give rise to the risk of thrombus or emboli.

Dehydration.

125. I have already dealt with what I consider to be the extent of the Claimant's dehydration. In the experts' Joint Statement, it was agreed that his dehydration could have been prevented by earlier transfusion, proper management of his fluid input and output and avoidance of the use of Frusemide.

126. As to the effects of the Claimant's dehydration, Dr Telfer's evidence was that dehydration would have reduced the liquid component of his blood, caused concentration of solutes in the blood, reduced plasma volume, resulted in an increased haematocrit (i.e. volume percentage proportion of red blood cells to plasma in the blood) and would, therefore, have resulted in an increase of blood viscosity. It could thus lead to the formation of a thrombus. In oral evidence, Dr Telfer acknowledged that there existed no medical literature to support his view that dehydration was likely to have increased the risk of thrombo-embolism, but said that, in his view, most clinicians would consider that the fact was "self-evident".

127. Dr Telfer had pointed out, in the experts' Joint Statement, that the data concerning increased viscosity came from patients with abnormally <u>high</u> haematocrit whereas, during his time at Pembury, the Claimant's haematocrit had risen, but was <u>not</u> abnormally high. This obviously militated against dehydration having had that effect in his case. In oral evidence, however, Dr Telfer's view appeared to change. He observed that, by reason of his congenital conditions, the state of the Claimant's blood was never 'normal' in the usual sense but was "very unviscous with a haematocrit of 0.18-0.2". He said that, for that reason, the "normal" limits did not apply and the Claimant's haematocrit - contrary to what he had said previously - <u>was</u> abnormally high. He

suggested that, as the Claimant became dehydrated, his haematocrit became higher than usual, rising to 0.21 on 25 November.

128. When the Claimant's previous haematocrit levels were examined, however, that statement did not appear to be correct. Of the 11 available readings which could be found from the period between April 2002 and March 2004, four were within the normal limits of 0.36-0.44. The three lowest readings were taken in February 2003 (0.21), December 2003 (0.26) and March 2004 (0.26). During his time in Pembury, the Claimant's haematocrit levels were:

    24 November : 20.00hrs 0.10
    25 November : 22.30hrs 0.21
    26 November : 11.18hrs 0.19
    27 November : 14.00hrs 0.28

    Thus, there was no support for Dr Telfer's contention that the Claimant's haematocrit levels whilst in hospital were "abnormally high". In fact, they were for the most part lower than usual, meaning that his blood was likely to have been less, rather than more, viscous. As Dr Telfer observed in his evidence, low viscosity will "optimise the circulation".

129. In the experts' Joint Statement, Dr Bolton-Maggs had accepted that there is a link between dehydration and increased blood viscosity and indicated that, if the Claimant's stroke had been caused by thrombus or emboli, she was unable to exclude the possibility that dehydration was a factor. In an Amended Opinion, however, she expressed the view that, whilst dehydration may contribute to thrombosis, that would only be when the dehydration was severe, not when it was mild or moderate. She referred to her personal experience of a neonate with severe dehydration who had suffered an aortic thrombus, and to a published Paper involving one other neonate, also with severe dehydration. She was able to provide no other epidemiological evidence to support her assertion. However, like Dr Telfer, she considered that increased blood viscosity might be a risk factor where the haematocrit was very high (50-60). She correctly noted that the Claimant's was not.

130. Professor Kirkham agreed with Dr Telfer. In her Report, she relied on literature which demonstrated that dehydration was likely to be a risk factor, although only in the venous (as opposed to arterial) system. She asserted that it was also a risk factor in the arterial system but produced no literature in support of that assertion. In oral evidence, she relied on a Paper, *Arterial Ischaemic Stroke Risk Factors* by *Mackay et al* (2011). The Paper reported part of a Study which had been undertaken by the IPSS, of which she herself is a member. The purpose of the Study was to describe presumptive risk factors for childhood arterial ischaemic stroke (AIS) and cerebral venous sinus thrombosis and to explore their possible causative relationship with those conditions. A "presumptive risk factor" is a factor that it is believed might be causative of a condition, not a factor that is known to have a causative effect. One of the many presumptive risk factors used in the Study was dehydration. It was present in only a small number of cases (36 out of 658) and the authors of the Paper reached no conclusion as to whether there was likely to be any causative relationship between dehydration and AIS. The Paper therefore provided no support for Professor Kirkham's assertion that dehydration could be a risk factor in the arterial, as well as the venous, system.

131. Dr O'Callaghan acknowledged that there is good evidence that dehydration may have a rôle in venous sinus thrombosis affecting the brain, but said there was no such evidence for arterial ischaemic stroke. He explained that, since the *Mackay* Study had examined presumptive risk factors for venous sinus thrombosis, as well as for AIS, the inclusion of dehydration as one of the presumptive risk factors was because of its documented association with the venous, not the arterial, system.

132. Professor Kirkham did not accept that only severe dehydration could lead to stroke. She considered that, when dehydration is an ongoing process, it has a continuing, not a threshold, effect. She said that dehydration on a continuum will "favour" thrombosis. Dr O'Callaghan disagreed. He did not consider that there was any authoritative evidence that the level of dehydration suffered by the Claimant would have caused a stroke. He pointed out that mild/moderate dehydration is very common in children. He considered that, if it were connected with thrombus and stroke, one would expect to see many cases in hospitals and to find the fact documented in the medical literature.

Conclusions on dehydration

133. Dr Telfer and Dr Bolton-Maggs agreed that the data concerning increased viscosity and the risk of thrombus came from patients with abnormally high haematocrit levels and, at the Joint Meeting, Dr Telfer suggested that the Claimant's haematocrit had been lower than the levels seen in the literature. His later change of mind; his belated assertion that, far from not having abnormally high haematocrit, the Claimant did have abnormally high haematocrit; together with the fact that his assertion did not appear to be correct are matters which make it impossible for me to rely on his evidence about this issue. In contrast, Professor Bolton-Maggs pointed out correctly that the Claimant's haematocrit levels were not high and gave no indication that the blood was more than usually viscous.

134. Professor Kirkham sought to rely on the *Mackay* Study as support for the proposition that dehydration is a risk factor for thrombus and emboli in the arterial system. On a proper analysis, however, the Study provided no such support and there is no epidemiological evidence that dehydration is liable to cause thrombus or emboli or in the arterial system.

135. As to Professor Kirkham's thesis that dehydration is an ongoing process which has a continuing, not a threshold, effect on the blood vessels, I can see that it has its attractions. If it be right that dehydration at a severe level leads to increased blood viscosity and renders thrombus and emboli more likely, I can see that it is plausible that a significant (although not severe) level of dehydration continuing over a period might be a risk factor for causing ongoing slow flow, causing thrombus and emboli. However, a major problem with that thesis was identified by Dr O'Callaghan, who pointed out that, given the large number of children who suffer from mild/moderate dehydration, if increased blood viscosity and slow blood flow, with the attendant risks of thrombus, emboli and stroke, were potential outcomes, it would be very surprising if that fact had not been documented in the medical literature. As it is, the thesis is not supported by any epidemiological evidence.

136. The position in which I am left, therefore, is that there is no objective evidence which links dehydration at the level which the Claimant had during his stay in hospital with the development of thrombus, emboli or stroke and no evidence that there is a link

between dehydration and thrombus and emboli in the arterial, as opposed to venous, system. Since, for reasons I shall explain, I consider that the arterial, not the venous, system was involved in the Claimant's case, that is an important factor. Moreover, the laboratory evidence tends to show that, far from being abnormally viscous, the Claimant's blood was actually un-viscous.

137. The Claimant's answer is that dehydration will always be working with other factors. Therefore, it is said, it is not surprising that there is no relevant medical literature or other objective evidence. I shall return to that point later in this judgment. However, I do not consider that, on a balance of probabilities, moderate dehydration taken on its own had the effect contended for by the Claimant.

THE CLAIMANT'S CASE ON THE LOCATION OF THE EVENT THAT TRIGGERED HIS STROKES

138. As I have already indicated, the Claimant's primary case is that the nature of the event which triggered the occurrence of his strokes was endothelial dysfunction leading to the formation of thrombus and emboli in one of three areas, all below the basilar artery. The emboli would then have been carried further up through the circulation before causing the occlusion to the basilar artery and the damage in the posterior circulation and the brainstem.

139. In her Report, Professor Kirkham suggested that the likely source of the event which triggered the occurrence of the strokes was a thrombus arising (i) from a dissection (i.e. a tear within the wall of a blood vessel) of one of the vertebral arteries; (ii) from the heart; or (iii) from somewhere in the venous circulation, e.g. in the pelvis or one of the Claimant's legs. By the time of the trial, however, her preferred source was (iii), i.e. a deep vein thrombosis (DVT) in the left leg. Failing that, she suggested that the thrombus must have formed in the heart or in one of the vertebral arteries somewhere below the basilar artery.

140. It is necessary to consider the evidence relating to each of those contentions.

DVT in the left leg

141. In support of her first choice of source, Professor Kirkham relied primarily on the clinical note written by Dr Kisat and timed at 15.30hrs on 27 November, which recorded that the Claimant had been complaining of "pain in left knee and leg" since the morning. Professor Kirkham was insistent that, if she had received such a complaint of pain, she would have immediately arranged a Doppler scan to ascertain whether there was a DVT. Her evidence was that thrombi in the deep veins of the legs are common in both adults and children who are not moving much; given that the Claimant was in bed, therefore, it was plausible that he might develop a DVT. She pointed out that no other reason for the leg pain had been identified.

142. Dr O'Callaghan's evidence was that DVT in a child is very rare. In any event, the location of a DVT was likely to be the calf or thigh, not the knee, which was the area specifically referred to in Dr Kisat's note. He also pointed out that the usual clinical signs of DVT, i.e. swelling and redness, did not appear to have been present at the time of the examination on 27 November by Dr Kisat. Dr Kisat had noted that, when examined, the Claimant had "normal limb movements" which did not suggest that he

had noticed anything untoward. Dr O'Callaghan pointed out that the Claimant's family also did not appear to have noticed any signs of swelling or redness.

143. In addition, Dr O'Callaghan pointed out that, in order to pass into the vertebro-basilar artery from the leg, the thrombus would have had to travel from the venous into the arterial circulation. From the right hand side of the heart, it would have had to pass into the left hand side of the heart. In order to be able to go across the heart, two factors would have had to be present. First, the Claimant would have had to have a patent foramen ovale (PFO). Every foetus has a PFO in order to obtain blood from the placenta and, usually, it closes after birth. However, research at post-mortem has revealed that 25%-35% of adults still have a PFO. The presence of a PFO can be ascertained by means of a transthoracic echocardiogram (TTE) or an alternative method which involves general anaesthetic. A TTE of the Claimant's heart was done at King's on 3 December 2004, after which a Senior Paediatric Registrar reported that it revealed that there was no PFO. There was no reason for the technique involving general anaesthetic to be used in the Claimant's case.

144. Professor Kirkham insisted that the TTE did not exclude the existence of a PFO. She was adamant that, on the balance of probabilities, there must have been a PFO, which would have been evident if a more sophisticated TTE (using agitated saline contrast) had been undertaken. Although there was no indication in the note of the King's TTE as to whether saline contrast had been used, she professed to be sure it had <u>not</u> been used because it was not noted. Dr O'Callaghan's view was that, given the percentage of adults known to have PFOs and the fact that the TTE showed no PFO, it must be probable that the Claimant did not have one.

145. Dr O'Callaghan also emphasised the need, if a thrombus is to pass from the right to the left of the heart, for there to be higher pressure on the right side than on the left, so that a reverse pressure gradient ('shunt') would be necessary. He said that there was no evidence of the presence of a shunt and, indeed, the fact that the Claimant was hypocapnic meant that he would have had less pulmonary artery pressure which made it even less likely that there would be one. Professor Kirkham disagreed and postulated that, although it was "hard to know", it was likely that there was higher pressure on the right side of the Claimant's heart. She explained the lack of any sign of the shunt on the TTE by saying that it was difficult to test for a right-to-left shunt in a two year old child.

146. I found Professor Kirkham's evidence supporting the likelihood of a DVT unconvincing. It rested primarily on one note of pain in the "left knee and leg". Although it is possible that "leg" <u>might</u> have referred to the thigh or calf, the reference to "knee" does not immediately suggest, as one would have expected, that the pain was in those areas. The Claimant's parents do not report specific pain in the leg on 27 November, nor have they described noticing the swelling or redness that would have been typical of a DVT. It appears clear from Dr Kisat's note that he did not observe any such signs. Nor was I told that any signs had become evident after the Claimant's transfer to King's. It is true that no alternative explanation has been given for the pain but it seems unlikely, given the other problems being suffered by the Claimant at the time, that such an explanation would have been actively sought. Furthermore, having regard to the condition of the Claimant on 27 November, it would perhaps not be surprising if he had suffered pain in various parts of his body, including his leg.

147. If the Claimant did not have a PFO, a thrombus could not have travelled from the leg, through his heart and into the vertebro-basilar circulation. I accept that it has been shown that a significant minority of people still have a PFO, even in adulthood, so it may be that the Claimant's PFO was still patent. However, the great majority of adults do not have a PFO and the King's TTE was reported as showing that no PFO was present in the Claimant's case. I find it difficult to see how, on the basis of that evidence, Professor Kirkham could say that the Claimant "probably" had a PFO. On the contrary, the probability is that he did not. Similarly, her view about the presence of a shunt was not supported by the evidence. The King's TTE showed no signs of a shunt and her explanation for the view that the TTE had given an incorrect impression was once again speculative.

148. I note also that Dr Telfer did not support Professor Kirkham's thesis, saying that DVT was not his "preferred mechanism", whilst, at the experts' Joint Meeting, Dr Bolton-Maggs agreed with Dr O'Callaghan, saying that the idea of thrombosis from the systemic circulation was "speculative" since that mechanism of stroke is "vanishingly rare" in children. Professor Kirkham acknowledged that DVT in children "is not thought to occur", but said "it does happen but people do not look for it." Her basis for making that assertion was not clear. I note also that, in her original Report, Professor Kirkham did not indicate that she considered that a DVT in the leg was the most likely source of the thrombus, merely identifying it as the third of three possibilities. The impression I received was that, having at some stage reached the clear conclusion that the source was a DVT, she was struggling to explain the evidence which militated against that explanation.

The heart

149. Although Professor Kirkham advanced as her second possibility the fact that a thrombus may have formed in the heart, neither she nor Dr O'Callaghan favoured that explanation. Dr O'Callaghan pointed out that, if that were the case, one would have expected some structural abnormality of the heart to be evident on the King's TTE. However, no such abnormality was seen. Nor was there any evidence of the Claimant having a predisposing factor for forming a clot in the heart. I do not consider that there is any reason to conclude that the heart was the source of the thrombus. The evidence which does exist tends to point the other way.

The vertebral arteries

150. Professor Kirkham's third suggestion was that a thrombus may have originated in one of the vertebral arteries below the basilar artery. She said that it was not possible to be sure, because there was inadequate imaging of the vertebral arteries, but the possibility could not be excluded. As to location, this was consistent with Dr O'Callaghan's opinion, which was that the original source of the arteriopathy which he considered had triggered the strokes was in the vertebro-basilar system, probably the vertebral artery. It was not of course consistent with his view as to the mechanism by which the strokes occurred or the cause thereof.

151. I have rejected the first two suggestions put forward by Professor Kirkham. Were I to accept that the strokes were caused by endothelial dysfunction, I would regard it as probable that the dysfunction occurred in the one of the vertebral arteries.

THE DEFENDANT'S CASE ON CAUSATION

152. In its Defence, the Defendant stated that the underlying cause of the Claimant's strokes was a cerebral arteriopathy caused by a viral infection. At the experts' Joint Meeting, Dr O'Callaghan expressed the view that the infection had been caused by inflammation or dissection of the vertebro-basilar vessels. In oral evidence, he explained that he believed that thrombus had then broken off and embolised upwards, causing occlusion of the basilar artery and the abnormalities of the posterior cerebral artery seen on the radiological imaging. It is to be noted that the involvement of dissection, thrombus and emboli is common to the cases of both parties, although that does not appear to have been appreciated, certainly on the Claimant's side, until Dr O'Callaghan's evidence was given at trial.

The relationship between focal cerebral arteriopathy and infection

153. Dr O'Callaghan's evidence was that viral infection, in particular URTI, is a major risk factor both for the development of focal cerebral arteriopathy and for stroke in childhood. In support of this assertion, he referred in particular to two pieces of medical literature. The first of these was *Predictors of Cerebral Arteriopathy in Children with Arterial Ischaemic Stroke, Results of the International Paediatric Stroke Study*, by *Amlie-Lefond et al* (2009), a Study which examined data relating to 525 children who had suffered arterial ischaemic stroke (AIS) and who had known vascular imaging results. The Study sought to test a number of predictive risk factors for childhood stroke. It found that the only significant predictor of focal cerebral arteriopathy as a cause of stroke was a recent URTI. The number of children who had focal cerebral arteriopathy was a relatively small proportion of the total cohort of the Study but, in the cases where there was focal cerebral arteriopathy, URTI appeared to be a significant factor.

154. The Conclusions in the Abstract state:

> "Arteriopathy is prevalent among children with arterial ischemic stroke, particularly those presenting in early school age, and those with a history of sickle cell disease. Recent upper respiratory infection predicted cerebral arteriopathy and FCA *(focal cerebral arteriopathy)* in particular, suggesting a possible role for infection in the pathogenesis of these lesions."

155. The Study contains this analysis:

> "Infection could contribute to stroke by promoting systemic procoagulant effects and local inflammation (or even direct pathogen invasion) of cervical or cerebral blood vessels. The pathogenesis of stroke in the setting of sepsis may be related primarily to the systemic procoagulant mechanism, which would explain the lack of association between sepsis and arteriopathy in our study. In children with recent URI *(upper respiratory infection)*, on the other hand vascular injury mechanism also may be at play …

> In the adult atherosclerosis literature, the concept of an infectious burden has been proposed whereby the cumulative inflammatory effects of multiple infections over time lead to vascular injury. This concept is a compelling potential explanation for arteriopathy in children, who suffer frequent minor infections yet rarely suffer strokes. Elevated inflammatory markers (C-reactive protein and erythrocyte sedimentation rate) and recent infection have been associated with vascular pathology in children, lending indirect support to this hypothesis."

The Study concludes that:

> "Arteriopathy is common in children with AIS and is associated with early school age, sickle cell disease, and recent URI. Although it may represent the end point of a variety of pathogenetic mechanisms, FCA is the most common type of arteriopathy observed and is associated with recent URI. Further studies are needed to explore this relationship between infection and arteriopathy in children, including questions regarding timing, specific infectious agents, inflammatory mediators, and cumulative effects or infections over time. Because recent data suggest that arteriopathy is the strongest predictor of recurrent childhood stroke, a better understanding of the infectious and inflammatory mediators of the vascular injury pathway is critical for the development of rational strategies for secondary stroke prevention in children."

Dr O'Callaghan said that this Study supported his view that even a minor infection was capable of causing arteriopathy and consequent stroke.

156. The second Paper relied on by Dr O'Callaghan was *Recent Trauma and Acute Infection as Risk Factors for Childhood Arterial Ischemic Stroke*, by *Hills et al* (2012), a Study published by the American Neurological Association. In explaining their objective, the authors of the Study stated that: "Trauma and acute infection have been associated with stroke in adults, and are prevalent exposures in children." The *Hills* Study was intended to explore whether those two factors (i.e. trauma and acute infection) were independently associated with childhood AIS. It was reported as showing that:

> "A medical encounter for a minor acute infection (prior 4 weeks) was … an independent risk factor …No single infection type predominated."

157. The *Hills* Study found that an out-patient medical encounter for a minor acute infection increased a child's risk of AIS more than fourfold. Even taking into account the fact that the parents of children with some chronic diseases associated with AIS might have a lower threshold for seeking medical care for a minor infection than the parents of normal children, the risk was still just less than fourfold. The most common infectious diagnosis among the cases was URTI (33%). The type of infection involved was described thus:

> "Recent minor infection was defined as a documented outpatient medical encounter for infectious illness within 4 weeks preceding the stroke/index date; time windows for infectious exposure in adult stroke studies have varied from 1 week to 20 months, but most were within 4 weeks. Minor infectious illnesses included acute fever attributed to infection by the treating physician, upper respiratory tract infection, pneumonia, acute otitis media, pharyngitis, urinary tract infection, and acute gastroenteritis."

Dr O'Callaghan considered that the increased risk of around fourfold was highly significant and that it demonstrated that there was a "robust relationship" between URTI and FCA.

158. In oral evidence, Professor Kirkham contended that the only virus for which there is any scientific support that it can cause focal cerebral arteriopathy is chickenpox. However, she accepted that there was clear epidemiological evidence showing that infection, in particular URTI, is a risk factor for childhood stroke. In his Report, Dr Telfer said that viral infection is a recognised, but rare, cause of vasculopathy and stroke, but only in the case of specific types of infection and more than a month after clinical presentation of the infection. Those assertions do not appear consistent with the literature to which I have referred. In his oral evidence, Dr Telfer acknowledged that infection would be a pro-thrombotic factor and that, if infection caused inflammation to a vessel wall, it would increase the risk of thrombosis. However, he did not consider that, without other pro-thrombotic factors, it would cause stroke.

Involvement of the posterior, rather than the anterior, circulation

159. During their Joint Discussion, the two Neuroradiologists were asked to consider whether vasculopathy caused to the cerebral arterial vessels by a viral infection (i.e. the Defendant's case) or emboli travelling from some other part of the circulation (the Claimant's case) was the most probable cause of the abnormalities seen on the radiological imaging. They made clear that the imaging could not differentiate between the two possibilities and said that they would defer to clinical opinion as to whether the cause of the abnormalities was more likely to be one or the other. However, they did observe that involvement of the vertebro-basilar (i.e. posterior) circulation was unusual for a vasculopathy, which more commonly affects the anterior circulation.

160. Dr Chong accepted that the imaging to some extent supported the theory that the underlying process causing the strokes was infection giving rise to focal cerebral arteriopathy. However, he considered that the involvement of the posterior, rather than the anterior, circulation was a factor which militated against that explanation.

161. Dr O'Callaghan's evidence was that arteriopathy is known to occur in the posterior, as well as the anterior, circulation, In support of his assertion, he relied again on the *Amlie-Lefond* Study. A Table of Baseline Characteristics of the 277 children included in the Study who had arteriopathy and for whom there was vascular imaging showed that, in 73% of cases, the anterior circulation was involved. The posterior circulation was involved in 20% of cases. Seven per cent of cases had involvement of both areas. On the face of it, therefore, the Study appears to suggest that, although a substantial

majority of cases involve the anterior circulation, a significant minority involve the posterior area.

162. Dr Chong's evidence was that the *Amlie-Lefond* Study had used a wide definition of "arteriopathy" and this had 'muddied' a proper understanding of the results. He pointed out that the definition used included cases of dissection, often dissection caused by trauma. He said that, in cases of dissection, involvement of the posterior cerebral circulation is more common. Also included in the definition used in the Study were inherited disorders, including SCD. That, he suggested, also accounted for the relatively high incidence of involvement of the posterior circulation.

163. Dr O'Callaghan relied also on an article, *Basilar Artery Stroke in Children*, by *Simonetti et al* (2012) published in Developmental Medicine for Child Neurology. The opening paragraph of the article states:

> "Only 10 to 30% of paediatric arterial ischaemic strokes … occur in the posterior circulation. Arteriopathies are the most frequent cause of posterior circulation stroke in children."

That was a Study of only 97 children, but again suggested that a significant minority of childhood arteriopathy occurs in the posterior circulation.

164. In her Report, Professor Kirkham relied on a Study, *The Course and Outcome of Unilateral Intracranial Arteriopathy in 79 Children with Ischaemic Stroke*, by *Braun et al* (2009) in support of her contention that :

> "Transient or focal cerebral arteriopathy, which may follow on upper respiratory tract infection … typically affects the distal internal carotid and proximal middle anterior cerebral arteries (Braun et al 2009), not the vertebro-basilar circulation."

Professor Kirkham failed to make clear that the *Braun* Study had <u>excluded</u> patients who had suffered injury to the vertebro-basilar circulation and thus did not provide any support at all for her statement. I accept that, as she explained when cross-examined, she had not intended deliberately to mislead, but it was an unfortunate error and did not inspire confidence. In the experts' Joint Statement, Professor Kirkham said that she had not been able to find any well-documented cases of viral vasculopathy in the posterior circulation and she had no experience of it herself.

165. I consider that the literature clearly shows that arteriopathy occurs in the posterior circulation, albeit in only a significant minority of cases. I do not find Professor Kirkham's insistence that she does not herself know of any case of focal cerebral arteriopathy occurring in the posterior circulation compelling. Even the *Braun* Study did not say that focal cerebral arteriopathy <u>never</u> occurred in the posterior circulation; it merely said that it "typically" affected other areas. As to Dr Chong's reservations about the definition of "arteriopathy" used in the *Amlie-Lefond* Study, I note that the Defendant's case is that the arteriopathy in the Claimant's case probably caused dissection which, according to Dr Chong, more commonly involves the posterior circulation.

Period of time between infection and stroke

166. The Neuroradiologists agreed that arterial ischaemic infarcts caused by viral infection tend to occur late, rather than early, in the natural history of the illness. Dr Chong believed that this was another factor which militated against the suggestion that infection had caused the Claimant's strokes. Dr Telfer agreed with Dr Chong. His evidence was that focal cerebral arteriopathy is usually a late complication of viral infection (most commonly chickenpox), developing many weeks or months after such infection.

167. Dr O'Callaghan relied once again on the *Hills* Study, which stated:

> "In our cohort, a medical encounter for a minor acute infection was the most frequently observed childhood AIS risk factor, present in 33% of cases. Because our definition of recent infection required a documented medical encounter, the true prevalence of this risk factor is higher, as many minor infections do not result in a medical visit. However, hospital series and an international prospective registry study have reported preceding minor infections (by parental report) in 24 to 34% of cases. The strength of the association between recent infection and AIS observed in our study (adjusted OR, 3.9) was similar to that reported in the adult studies, ranging from 2.9 (95% CI, 1.6-5.3) for an infection in the prior 2 months to 4.5 (95% CI, 2.1-9.7) for an infection in the prior week."

He pointed out that, whilst the *Hills* Study showed that a child who had had a minor acute infection within the previous four weeks had more than a fourfold risk of suffering an AIS, the authors considered that this risk factor was, in reality, higher because many minor infections do not result in a medical visit and such cases would not, therefore, have been included in the Study. Dr O'Callaghan said that the *Hills* Study supported his view that a minor infection of only recent onset was capable of causing arteriopathy.

Conclusions on the relationship between focal cerebral arteriopathy and infection

168. I consider that the literature relied upon by Dr O'Callaghan provides clear objective evidence about the risks associated with infection, even a minor infection which has been present for only a short period before arteriopathy occurs. The fact that a child suffering from a minor acute infection has more than a fourfold risk of an AIS is, as Dr O'Callaghan observed, a highly significant finding.

The site of the focal cerebral arteriopathy, if it occurred

The neuroradiological evidence

169. In his Report, Dr Forbes expressed the view that the extensive abnormalities of the vertebro-basilar circulation which he said were evident on the MR imaging of 28 November were consistent with an underlying occlusive arterial disorder, i.e. a vasculopathy. He also expressed the view that the April 2005 MR imaging, which was of better quality than the 28 November 2004 MRI scan, confirmed the abnormalities

previously seen and, because the basilar artery was now visible, showed irregularities, in particular irregularities of the lumen, at the distal end of the basilar artery and in the posterior cerebral artery. He considered that the MR images were again consistent with a vasculopathy which was probably caused by or was a manifestation of some unspecified infective or immunological process.

170. In oral evidence, Dr Forbes advanced his theory further, expressing the view that the thrombus had formed initially in the terminal part of the vertebral artery and extended into the basilar artery. He considered that, although the basilar artery was still open at the time of the CT scan, both the basilar and the vertebral arteries may have been affected in some way at that stage. He attributed the irregularities which he had identified in the April 2005 MRI images to the historic result of the end stages of the process which had occurred in November 2004, when the underlying arteriopathy had caused thrombus to form and to embolise in the vertebro-basilar circulation.

171. Dr Chong considered that there were no irregularities of the lumen; he pointed out that the MRI scan looked only at the flow of blood. Therefore, he said, it was not possible necessarily to conclude that poor flow meant the lumen had become narrowed. He acknowledged that the imaging did show a disturbance of flow and that one reason might be narrowing of the lumen, but he said that there were many other possible reasons. He accepted that, if the abnormality was not caused by flow, but by damage to the lumen, one could conclude that there had been arteriopathy. He conceded that such arteriopathy could have been caused by infection, although he said that there could also be a number of other possible causes. Dr Forbes considered that the MR images suggested irregularity of the lumen, rather than poor flow, because, if there was poor flow, it would have had a more regular appearance. He accepted that there was no definitive evidence of damage to the lumen but he did not regard the appearances of the images as inconsistent with his view.

172. I accept the evidence of Dr Chong on this point. As I have previously indicated, Dr Forbers' misinterpretation of the images of the anterior circulation makes me cautious about preferring his evidence relating to the abnormalities evident in the distal basilar artery and the posterior cerebral artery to that of Dr Chong. I therefore accept the latter's evidence that what was evident on the imaging was blood flow, rather than irregularities of the lumen.

173. At the stage of final submissions, Mr Post suggested that there were significant weaknesses and inconsistencies in the Defendant's approach to the neuroradiological evidence. As I have already observed, he criticised Dr O'Callaghan for not being more specific about what he believed was the precise position of the arteriopathy which he was saying had caused the Claimant's strokes. He emphasised that there was no radiological evidence of arteriopathy in the vertebral arteries and that Dr Chong had been cross-examined only in respect of the abnormalities in the distal basilar artery and the left posterior cerebral artery. He pointed out that, in his evidence, Dr Forbes had also focussed on those areas and had said that he had not seen irregularity in any vessels other than the basilar and posterior cerebral arteries.

174. The problem with that approach was that the CT and MRI scans did not show the whole picture. Dr Chong observed that the MR image quality of the left vertebral, basilar and left posterior cerebral arteries was limited in the 28 November 2004 MRI scan, whilst Professor Kirkham said in oral evidence that "we are hampered by the lack of imaging"

and “We don’t have good images anyway of the whole of the vertebral”. Thus, it was not possible for Dr O'Callaghan to be certain of the site of the arteriopathy, if it occurred. In particular, it was not possible for him or anyone else to state positively that the arteriopathy (on the Defendant’s case) or the endothelial dysfunction (on the Claimant’s case) occurred in one of the vertebral arteries or elsewhere in the system.

175. Mr Post also criticised Dr O'Callaghan for claiming in his oral evidence that the Claimant’s viral infection had caused the arteriopathy “as seen on the imaging” and for saying that the interpretation of the radiologists was that there was “abnormality of the vertebral and basilar arteries”. In cross-examination, Dr O'Callaghan explained that he had been referring to the multiple infarcts and radiological abnormalities in the vertebro-basilar arteries which he considered would be consistent both with arteriopathy (the Defendant’s case) or endothelial dysfunction (the Claimant’s case) and thrombus. He made clear that he had not been referring to findings in specific locations. I do not consider that the criticisms of Dr O'Callaghan were justified. He at no time claimed to know precisely where the event which triggered the Claimant’s strokes occurred. He merely expressed his view as to where he considered most likely.

176. The Neuroradiologists at no time suggested that the site of the abnormalities which they had seen on the MR imaging was determinative of the causation issue. The evidence of each of them was that the radiological picture was consistent with his preferred option, although neither contended that it was inconsistent with the opposing view. Dr Chong accepted that the imaging to some extent supported the suggestion that there had been vasculopathy caused by infection. However, he raised the reservations about the involvement of the posterior circulation and the timing of the infection to which I have already referred. He also expressed his view that stroke tends to be caused by multiple factors acting synergistically, rather than by one factor such as infection. I will return to that issue in due course. He did not, however, suggest in evidence that the abnormalities seen in the imaging meant that there could not have been an arteriopathy in the vertebral artery. Dr Forbes also accepted that the radiological evidence would support the Claimant’s case although he expressed reservations about the suggestion that there had been a DVT.

The site within the vertebro-basilar circulation

177. It appeared to be common ground that, if focal cerebral arteriopathy caused by infection occurred, it would have originated in the posterior cerebral artery, the basilar artery or the vertebral artery.

178. In their Joint Discussion, the Neuroradiologists were asked to consider whether there was any evidence to suggest that occlusion of vessels had occurred between the time of the CT scan and the first MRI scan. They agreed that, at the time of the CT scan, there was enhancement of (and therefore blood flow in) the upper part of the basilar artery, but that there was apparent absence of flow in that area on the later MRI scan. The experts agreed that this may represent an evolving occlusion. It certainly appears to suggest that the site of the event which triggered the strokes, whether arteriopathy or endothelial dysfunction, occurred below the basilar artery.

179. Neither Professor Kirkham nor Dr O'Callaghan considered that the event occurred in the posterior cerebral artery. There is no doubt that the basilar artery became occluded

and, since it is below the posterior cerebral artery, it is difficult to see how this could have happened had the posterior cerebral artery been the source of the original event.

180. As to the basilar artery, Professor Kirkham's view was that, if there had been arteriopathy there, it was difficult, because of the large size of the basilar artery, to see how the artery could have been occluded completely and for so long as to cause the degree of damage suffered by the Claimant. Furthermore, the absence of flow in the upper part of the basilar artery visible in the 28 November 2004 MRI scan meant that the source must have been lower down. Dr O'Callaghan also did not consider that the source was in the upper part of the basilar artery. He considered that the most likely place was the vertebral artery or the vertebral artery extending into the basilar artery.

181. Professor Kirkham's evidence was that, if the term, "focal cerebral arteriopathy" was taken to include "dissection", it was possible to have focal cerebral arteriopathy causing multiple emboli from a nidus (i.e. focus of infection) in the vertebral artery. She was reluctant to accept that such arteriopathy could be caused by URTI. However, she did acknowledge that a vertebral dissection with thrombus formation was "one reasonable alternative" explanation for the Claimant's injuries. She accepted also that the suggestion could not be excluded because of the lack of good quality imaging and agreed also that dissection could occur but not be capable of detection on CT and MRI imaging. Despite her acceptance of this possibility, however, Professor Kirkham's evidence was that the mechanism was unlikely because of the extensive nature of the Claimant's brain damage. I will deal with that issue in due course.

182. As to the issue with which I am currently concerned, if a focal cerebral arteriopathy did occur, I consider it probable that it was in one of the vertebral arteries. It may or may not have resulted in abnormalities visible on good quality MR imaging. As it is, because of the poor quality of the available images, it is impossible to be sure. However, I accept Dr O'Callaghan's evidence on this point and note that Professor Kirkham conceded that it was possible, albeit expressing reservations because of the extent of damage caused. It is notable that the site which was originally Professor Kirkham's first choice for the occurrence of endothelial dysfunction was also Dr O'Callaghan's preferred site for arteriopathy.

The extent of the damage

183. Professor Kirkham considered that, if the focal cerebral arteriopathy had involved one of the vertebral arteries, the blood flow would have been maintained by the other vertebral artery and it would not have resulted in multiple infarcts. She did not consider that arteriopathy secondary to infection could have caused such a large thrombosis to so many arteries without the additional factors of dehydration and anaemia. She said that, in her clinical experience, cases where focal cerebral arteriopathy occurring in the vertebral artery had led to the propagation of thrombus, embolisation of the basilar artery and infarction in the posterior cerebral artery had been very rare. Usually, whilst a stroke might occur, the arteriopathy will not produce so many emboli or cause such seriously disabling consequences. In her experience, there is usually less extensive damage, with a more favourable prognosis. She attributed the damage to the Claimant's brainstem and his severe disability to the effects of the basilar occlusion which had occurred; she said that extent and kind of occlusion is very unusual in children.

184. Dr O'Callaghan did not consider that the extent of the damage or the level of the Claimant's disability was determinative of the question of whether his stroke was likely to have been caused by focal cerebral arteriopathy, rather than endothelial dysfunction. He accepted that, if the strokes had been cerebellar, the Claimant would probably have recovered well. However, he said that, given that the basilar artery was occluded and damage was caused to the brainstem, severe disability was to be expected.

185. I accept Dr O'Callaghan's evidence on this issue. It does not seem to me that the extent of the damage to the Claimant can be regarded as determinative of the cause of that damage. The Neuroradiologists did not suggest that was the case. Moreover, one of Professor Kirkham's suggested sites of endothelial dysfunction was one of the vertebral arteries. If it be right that the dysfunction could occur there and cause the injuries suffered by the Claimant, I do not see how, if arteriopathy occurred at the same site, the same could not be true.

ISSUES OF LAW

186. Before proceeding to deal with my conclusions, there are two issues of law to be addressed. The first relates to the scope of the duty of care owed to the Claimant by the Defendant. The second relates to the Claimant's secondary case, namely that, even if the effects of the delay in transfusion and the other breaches of duty did not constitute the sole cause of his strokes, they made a material contribution thereto.

The scope of the duty of care

187. The Defendant argued that, even if I were to find that the Claimant's strokes and consequent brain damage had been caused or materially contributed to by the Defendant's breach of duty, the damage would be too remote from that breach of duty to be within its scope and not reasonably foreseeable.

188. In making that submission, the Defendant relied on the decision of the Court of Appeal in the case of *Brown v Lewisham and North Southwark Health Authority* [1999] Lloyds LR 110. In that case, the Claimant (described as "plaintiff") had undergone quadruple coronary artery bypass surgery at a London hospital. The surgery had gone well but he had been given prophylactic anti-coagulant treatment with heparin and had developed a DVT in his left leg which had not been detected. He was discharged from the hospital to travel by taxi and train to another hospital in Blackpool. At the time of his transfer, he was suffering from a chest infection and, for that reason, it was accepted that his discharge had been negligent. Once in Blackpool, the DVT was diagnosed and the Claimant was again treated with heparin. He developed an adverse reaction to the heparin and, as a result, suffered a worsening of his DVT which ultimately resulted in the loss of his leg.

189. The judge at first instance found against the Claimant on the issue of causation on the ground that, even if he had not been discharged from the London hospital, the DVT would have continued to develop and he would have been treated with heparin as in fact occurred. The Court of Appeal dismissed the Claimant's appeal against that decision. In giving judgment, Beldam LJ raised a significant point *obiter*:

> "[*Counsel for the Plaintiff's*] argument assumed that, as the first defendant had admitted a breach of duty, it remained only for the plaintiff to prove a causal connection with the damage

> he had suffered. In the light of my view that no such connection has been shown, it is unnecessary to say whether this assumption is correct but I would certainly question it. It was said that, if a defendant is in breach of duty, it is no defence that the plaintiff suffers damage in an unforeseeable way; the defendant has to take the plaintiff as he finds him provided that the damage is of the same type, i.e. personal injury. The paradigm example is the plaintiff with the eggshell skull. So [*Counsel*] argued, the first Defendant had to take [*the plaintiff*] with his undetected DVT and his rare but not unforeseeable reaction to heparin. The doctor's duty was to take care for the health of his patient. If he is in breach of that duty it does not matter that injury to health occurs in an unforeseeable way.
>
> For the purpose of analysis it may sometimes be important to be more precise in the definition of duty. A doctor is obliged to exercise the care and skill of a competent doctor. He must take care in the examination, diagnosis and treatment of his patient's condition to prevent injury to his health from risks which a competent practitioner would foresee as likely to result from his failure to do so. He is not a clairvoyant nor if he tells his patient that he can find nothing wrong is he liable if his patient has a condition which was not discoverable by competent examination. The public policy of limiting the liability of tortfeasors by the control mechanism of foreseeability seems to me as necessary in cases of medical as in any other type of negligence. I do not see on what policy ground it would be fair or just to hold a doctor to be in breach of duty who failed to diagnose an asymptomatic and undetectable illness merely because he was at fault in the management of a correctly diagnosed but unrelated condition. In short it must be shown that the injury suffered by the patient is within the risk from which it was the doctor's duty to protect him. If it is not, the breach is not a relevant breach of duty."

190. Mr Moon argued that Beldam LJ's observations were apposite in this case. He pointed out that there is no medical literature which suggests an association between delay in performing a blood transfusion, and/or the other breaches of duty which I have found, and stroke. Thus, he submitted, the occurrence of the strokes and the brain damage resulting therefrom are too remote from the breaches of duty to be within their scope. These were, he suggested, not injuries within the risk from which it was the Defendant's duty to protect the Claimant.

191. Mr Post argued that it was not necessary that the Defendant must have foreseen the particular mechanism of injury. He relied on the evidence of Dr Becker, who was asked in cross-examination about the risks which a Paediatrician would have anticipated in the event that the Claimant's transfusion was not performed promptly. He said that, if a small child like the Claimant with very low haemoglobin becomes unwell, a wide

variety of complications can occur. Those complications would include cardiac problems, with the resultant possibility of brain damage. His evidence was that the range of complications a Paediatrician would be seeking to avoid by carrying out a transfusion would be very wide.

192. Mr Post relied also on the case of *Stephen Loraine v Wirral University Teaching Hospital NHS Foundation Trust* [2008] EWHC (QB). In that case, the Defendant had negligently failed to admit the Claimant's mother to hospital prior to the birth of the Claimant despite the fact that she had a fibroid in her uterine wall and the foetus was in the 'footling' position. The Claimant's mother then suffered a profound placental abruption which resulted in the Claimant suffering foetal asphyxia, with consequent severe disability. The Defendant argued that it was not liable because the Claimant's injuries were caused by a mechanism which was not reasonably within the contemplation of those caring for his mother at the time when she should have been admitted to hospital. If she had been admitted to hospital, it would have been because there was a foreseeable risk of cord prolapse. It could not have been contemplated that she would suffer a placental abruption.

193. In *Loraine*, Plender J reviewed the authorities and referred in particular to the well known case of *Hughes v Lord Advocate* [1963] AC 837. In that case, employees of the Post Office, in breach of their duty, had left a manhole uncovered but placed paraffin lamps around it. In those circumstances, it was foreseeable that a child might suffer burns; the Claimant did suffer burns, although the mechanism by which he did so was entirely unforeseeable. He climbed down the manhole and, on ascending, knocked over a paraffin lamp which caused an explosion. The first instance Court found against the Claimant. The House of Lords reversed that decision. At 849, Lord Reid stated:

> "The appellant's injuries were mainly caused by burns and it cannot be said that injuries from burns were unforeseeable … No doubt it was not to be expected that the injuries would be as serious as those which the appellant in fact sustained. But a defender is liable although the damage may be a good deal greater in the extent than was foreseeable. He can only escape liability if the damage can be regarded as differing in kind from what was foreseeable."

Plender J applied that principle to the facts of *Loraine*. He said at paragraph 64 of his judgment:

> "In the present case, the damage suffered by the Claimant does not differ in kind from what was foreseeable. The damage foreseeable in the event of a cord prolapse is precisely the same in kind as the damage suffered by reason of the placental abruption. That damage is cerebral palsy in consequence of foetal asphyxia."

194. I consider that this case falls squarely within the decisions in *Hughes* and *Loraine*. It differs from *Brown*, where the existence of the Claimant's DVT and of the damage that might result from it was unknown to the doctors who discharged him from hospital.

The condition which meant he should not have been discharged, i.e. infection, was wholly different from the DVT and heparin intolerance which caused the loss of his leg. In this case, it is clear from Dr Becker's evidence that a competent Paediatrician should have foreseen that a failure to transfuse promptly would give rise to a risk, albeit a small risk, of cardiac problems leading to brain injury. The Claimant's case is that, as a result of the delay in transfusing, he suffered brain injury caused by strokes. The damage would be the same in kind as that which should have been foreseen, although the route by which he suffered the damage would not have been the same as the route that was to be foreseen at the time of the breaches. In the circumstances, therefore, I am satisfied that the Claimant's claim should not fail on that ground.

Material Contribution

195. The second issue is, I believe, uncontroversial. In the event that the Claimant does not succeed in establishing his primary case, he relies on the principle in *Bailey v Ministry of Defence et al.* [2008] EWCA Civ 883. In that case, the Claimant was admitted to a hospital managed by the First Defendant for treatment of a gall stone. Following surgery, she became weak and developed pancreatitis. She was sent to an intensive care unit and subsequently to the renal ward at another hospital managed by the Second Defendant. There, she was given a drink, vomited and was unable to clear her throat. She aspirated the vomit, causing a cardiac arrest which led her to suffer hypoxic brain damage. She claimed damages in negligence against both Defendants, contending, *inter alia*, that a lack of care by the First Defendant during her admission to its hospital had materially contributed to the cardiac arrest and consequent brain damage.

196. The judge at first instance found that the cardiac arrest had been caused by the Claimant's weakness on the date of her transfer to the Second Defendant's hospital. That weakness had, he found, two cumulative causes, i.e. the First Defendant's negligent lack of care during her admission at its hospital and her pancreatitis, for which it was not responsible. He held that, since the negligent lack of care had contributed materially to the Claimant's overall weakness, causation had been established and he accordingly found the First Defendant liable and dismissed the claim against the Second Defendant.

197. The Court of Appeal dismissed the First Defendant's appeal. Giving the judgment of the Court, Waller LJ set out the principle at paragraph 46:

> "In my view one cannot draw a distinction between medical negligence cases and others. I would summarise the position in relation to cumulative cause cases as follows. If the evidence demonstrates on a balance of probabilities that the injury would have occurred as a result of the non-tortious cause or causes in any event, the claimant will have failed to establish that the tortuous cause contributed. *Hotson's* case exemplifies such a situation. If the evidence demonstrates that "but for" the contribution of the tortuous cause the injury would probably not have occurred, the claimant will (obviously) have discharged the burden. In a case where medical science cannot establish the probability that "but for" an act of negligence the injury would not have happened but can establish that the

> contribution of the negligent cause was more than negligible, the "but for" test is modified, and the claimant will succeed."

198. That is the principle which I shall apply in the event when I consider the issue of material contribution in this case**.**

CONCLUSIONS

The Claimant's Primary Case

199. This case involves a large number of complex and uncertain medical issues. I have to consider carefully whether, on the evidence available to me, the Claimant has succeeded in establishing to the required standard that his injuries occurred in the manner set out at paragraph 30 of the Amended Particulars of Claim (see paragraph 81 of this judgment) and were therefore caused by the Defendant's breaches of duty.

200. I have already set out the evidence relating to hypoxia, hypocapnia and dehydration. That must be set against the background of the severe anaemia and haemolysis from which the Claimant was undoubtedly suffering during his time at Pembury. I have found that there is no convincing evidence that, in general, anaemia and haemolysis give rise to the risk of thrombus, emboli or stroke in the case of a patient who, like the Claimant, suffers from HS. I note also that Dr Bolton-Maggs, who in her work with SHOT, has daily experience of the problems arising from blood transfusion, observed that she was aware of no case in which a delayed transfusion had been identified as causing a stroke. As to hypoxia, I have found that there is no evidence that the Claimant was hypoxic at the material time; indeed the evidence points the other way. He was undoubtedly hypocapnic, but I have found that the protective mechanisms available to patients with HS are likely to have protected him from the vasoconstriction that can result from hypocapnia in a normal patient. As to dehydration, the Claimant's dehydration did not fall within the "severe" category and his haematocrit levels were low, suggesting that his blood was not unusually viscous. There is no authoritative evidence that patients with the Claimant's level of dehydration or with his haematocrit levels are prone to thrombus, emboli or stroke. Moreover, I have concluded that the endothelial dysfunction, if it occurred, was in one of the vertebral arteries, not the venous system, and there is no epidemiological evidence linking dehydration with the development of thrombus and emboli in the arterial system.

201. The Defendant has relied heavily on the absence of epidemiological evidence to support the Claimant's case. The point is made on behalf of the Claimant that his case is highly unusual. His congenital conditions, coupled with the severity of his anaemia on 24 November and the worsening of his condition caused by the delay in transfusion and his dehydration, has, it is suggested, produced a situation which is unlikely to be replicated in medical research. Of course, I recognise the force of that argument but, nevertheless, it is the case that many people suffer a combination of some or all of these conditions without suffering from strokes. It was also suggested that I should focus to a greater extent on the personal clinical experience of the Claimant's expert witnesses, rather than merely on the epidemiological evidence. However, whilst I do of course understand the importance of clinical experience, any decision I make must be founded on objective evidence (including authoritative medical literature, laboratory findings and clinical observations), rather than merely on personal opinions. I might of course accept the opinion of an expert on a particular issue. Before doing so, however, I must

be satisfied that it is reliable and well-founded. I am afraid that, in the case of the Claimant's haematological and paediatric neurological experts, I could not always be satisfied that that was so.

202. It was said on behalf of the Claimant that the combination of conditions from which he suffered combined, first to create a "pro-thrombotic state" and then, by the perturbation mechanisms set out in *Virchow's Triad*, to cause the endothelial dysfunction which triggered his strokes. I appreciate that there is a possibility that the various factors might have combined and acted cumulatively or synergistically to produce such an outcome. However, my attention was not drawn to any authoritative medical literature which confirmed the existence of such a cumulative or synergistic effect and, insofar as this explanation was advanced by the expert witnesses, I cannot be satisfied on the evidence that it is well-founded. I cannot merely assume that these factors operated to cause the Claimant's strokes. It follows, therefore, that the Claimant has not succeeded in establishing his primary case.

The Defendant's case and the Claimant's secondary case

203. For the Claimant, Mr Post argued that the Defendant's case, i.e. that the Claimant suffered arteriopathy as a result of infection, is purely speculative. He submitted that there was no evidence as to the precise nature of the infection from which the Claimant was suffering and how it came to cause his strokes. There had been no laboratory investigations into the infection at Pembury or at King's. Furthermore, there was no indication in the medical records that he was suffering from anything but an ordinary minor infection and there was no positive radiological evidence of the site of the arteriopathy.

204. In oral evidence, Dr O'Callaghan acknowledged that, assuming that infection had caused arteriopathy, the reason why it did so remained a mystery. He suggested that one possible explanation was that the Claimant had suffered the cumulative effects of his past infections in addition to the infection from which he was suffering on his admission to Pembury in November 2004.

205. As I have already said, there is clear evidence in the medical literature showing that a minor acute infection, in particular URTI, is a significant risk factor for arteriopathy and AIS. It is true that such an arteriopathy will usually affect the anterior, rather than the posterior, circulation, but it is nevertheless clear that there are a significant number of cases in which the posterior circulation is involved. It is also clear that it can occur even where an infection is very recent.

206. There is little doubt that, when he was first taken to Pembury on 24 November, the Claimant had a URTI from which he had been suffering for about a week. On that day, his condition had worsened and he had an increased temperature at 38°. He was described as looking poorly, worse than he usually did when his Hb level was low. I note that the diagnosis made by Dr Gika at the time of the Claimant's admission was "?viral infection causing deterioration of haemolytic anaemia". In other words, she considered the infection sufficiently significant to have caused his anaemia. What she did not know at that stage was that his Hb level had fallen to 3.3, i.e. the lowest it had ever been, by a considerable margin. The previous lowest level had been 4.2 in April 2003. The last incidence of infection previously recorded (which was described as "non-specific" and had caused the Claimant to "cough and wheeze") had been in

August 2004 when his Hb was 6.2. Even after the first transfusion on 25 November, when he was somewhat improved, the Claimant's temperature remained raised, presumably as a result of his URTI.

207. I do not consider that the fact that no specific virus was positively identified as a cause of the Claimant's strokes is significant. It seems to me that the overwhelming likelihood, if the Claimant developed an arteriopathy due to infection, is that the infection concerned was the URTI from which he was known to be suffering. Given the severity of the Claimant's condition during his last hours at Pembury and subsequently at King's, it seems unlikely that an investigation to discover the nature of that infection and/or to find out whether he had some other infection would have been regarded as a first priority. It certainly does not appear from the King's Discharge Summary that the existence of any other infection became evident during his stay there.

208. I am satisfied, on a balance of probabilities, that the primary cause of the Claimant's strokes was a focal cerebral arteriopathy which was in turn caused by the URTI from which he was suffering. Such an infection is a clearly established risk factor for arteriopathy and strokes in children, even when it is "minor", as it apparently was in the Claimant's case. I note that, at the Joint Meeting, the experts agreed that "such (i.e. such as his URTI) non-specific infections can be associated with stroke in children". As I have previously indicated, I do not regard the fact that an arteriopathy of the vertebral artery was not visible on the radiological imaging prevents such a conclusion. The same site was identified by Professor Kirkham for an endothelial dysfunction, the imaging of the vertebral arteries was not of good quality and, in any event, Professor Kirkham conceded that dissection could occur without being detected on imaging.

209. As to why the infection should have caused the arteriopathy, that is not clear. However, I note that the *Amelie-Lefond* Study (see paragraph 155) refers to the "concept" of an "infectious burden", whereby the inflammatory effects of multiple infections over time lead to vascular injury in adults. The Study suggests that it is a "compelling potential explanation for arteriopathy in children, who suffer frequent minor infections yet rarely suffer strokes". Although the cumulative effect is only said to be a "potential explanation", the view is expressed in an authoritative IPSS Study. The Claimant was very young, he had suffered a number of previous infections (one only three months before) and it appears from his Hb level on 24 November that this infection had had a particularly serious effect on his anaemia and his general wellbeing. The cumulative effect suggested by Dr O'Callaghan appears to be a very plausible explanation. Alternatively, it may be that the nature of the infection, although apparently everyday, was somehow different from those he had had before.

210. I come now to the question of material contribution. At paragraph 32 of the Amended Particulars of Claim, the Claimant contended that, in the event of a finding that focal arteriopathy was the primary cause of perturbation of the blood vessel wall, it would be asserted that his dehydration, acute-on-chronic haemolysis, severe anaemia and the use of diuretics (the effect of which relates to his dehydration) caused, or made a contribution to, the occlusion of the basilar artery and the consequent strokes.

211. Professor Kirkham considered that, if there had been focal cerebral arteriopathy, other factors must have been at play which resulted in the serious damage. Her evidence was that strokes in adults and children almost always have multiple risk factors interacting. She had come across cases where there was a single cause of stroke only very rarely.

She said that, in a case of stroke, she would always be looking for other risk factors. Dr Telfer's view was similar. He said that the cause of strokes is frequently multi-factorial, and is accepted as such by all Haematologists. Dr Bolton-Maggs accepted that, on occasion, strokes may be caused by different contributing factors, although she did not consider that the factors present in this case had a contributing effect.

212. Dr O'Callaghan's evidence was that there are few proven risk factors for stroke in children. SCD is one, as is viral infection. He did not accept that there is any proof that stroke is multi-factorial. He accepted that, when one looks at large cohorts of childhood strokes, it is possible to identify a number of presumptive risk factors in about half of cases. However, as I have previously noted, presumptive risk factors are factors that it is believed might be causative, not factors where there is any positive evidence of a causative effect. When asked whether the Claimant's strokes were likely to have been multi-factorial, Dr O'Callaghan acknowledged that there may have been other factors, e.g. genetic factors, at play although that was plainly speculative. He acknowledged also that there is some evidence that having more than one pro-thrombotic risk factor has an additive effect. However, he did not accept that dehydration, acute-on-chronic haemolysis and severe anaemia were pro-thrombotic factors or had played a part in causing the Claimant's strokes.

213. Mr Post pointed out that the Claimant had suffered a number of previous episodes of infection in the presence of anaemia, without suffering a stroke. He suggested that there was, therefore, no reason to believe that he would have done so in November 2004 without some additional factor. He suggested that the only plausible candidate for such an additional factor was the pro-thrombotic state likely to have been caused by the Claimant's dehydration, acute-on-chronic haemolysis and severe anaemia. He argued that, on a balance of probabilities, even if infection did cause arteriopathy as I have found, those conditions must at least have made a material contribution in causing his strokes.

214. Professor Kirkham's view that strokes in adults and children almost always have multiple risk factors interacting appeared to be based, not on the medical literature, but on her own assessment of causation in the (no doubt very many) stroke cases she has seen. Her evidence that, in a case of stroke, she "would always be looking for other risk factors" is not the same as positive evidence that there is always more than one cause. Similarly, Dr Telfer's assertion was not supported by any relevant literature. If it is right that all Haematologists accept that strokes are frequently multi-factorial, with some of those factors being conditions as common as anaemia and dehydration, one might expect to see that reflected in the textbooks and in other literature.

215. It may well be that a significant number of strokes occur as a result of a combination of factors, rather than a single cause. However, that fact alone does not assist me in determining whether the specific conditions from which the Claimant was suffering and which were caused by the Defendant's breaches of duty (in particular, the delay in transfusing him) made a material contribution to his injuries. I have to examine the evidence relating to those conditions and ascertain whether it establishes to the required standard that they had a contributory role.

216. In relation to that exercise, the Claimant faces similar problems to those which I referred to when dealing with his primary case. Once again, I accept that there is a possibility that the various conditions, or some of them, may have combined

cumulatively or synergistically with the arteriopathy to cause his strokes. However, there is no objective and reliable evidence that the Claimant's dehydration, acute-on-chronic haemolysis and/or severe anaemia, whether together or separately, contributed with the arteriopathy to cause his strokes. That being the case, I cannot reach the conclusion that it was so and the Claimant's secondary case must fail.

217. I recognise that my decision will be a great disappointment to the Claimant's family. The only consolation they can take from this litigation is the fact that they have done as much as they reasonably could in an attempt to secure his financial future.