780

HALL Rosemary

From: CROSS Billy
Sent: 07 April 2008 10:51
To: HALL Rosemary
Subject: : Report

Rosemary

See para 69 of Dr Evan's report. Contact Dr Herron and seek his opinion. It may be best to email the report to him if he can provide an email address.

If possible, need result by 0930 this Thursday. If he can report verbally give him my mobile no., or have him email you and you can phone me if I am away to Wales/

Billy

Brian Herron

[redacted]

1. I have prepared this report at the request of the Crime Operations Department Serious Crime Branch, Gough Barracks, Barrack Hill, Armagh, BT60 I BW.

2. I have received the following documents

i. Letter of Instruction dated 23.1.08.
ii. The original clinical casefile of Claire Roberts.
iii. Verdict on Inquest.
iv. A letter from Dr Walby dated 16.12.04
v. Two Statements from Mr Alan Roberts, Claire's father.
vi. Statement of Dr Maconchie
vii. Statement of Dr Sands.
viii. Statement of Dr. Young.
ix. Statement of Dr Steane.
x. Statement of Dr. Webb.
xi. Autopsy report Dr Herron.
xii. Neuropathology report of Dr Harding.

3. My instruction is to review the clinical history and the enclosed Statements, with regard to the death of Claire Roberts in October 1996.

Claire was a young girl of 9 years. She had long standing learning difficulties, and there was a query regarding attention deficit hyperactivity disorder (ADHD). She was otherwise in good physical health. She was admitted to the Royal Belfast Hospital For Sick Children on the evening of 21 Oct 96. Her condition deteriorated, and in the early hours of 23 Oct she collapsed and was found to have fixed dilated pupils. Resuscitation was unsuccessful and all treatment was withdrawn at 18:45 hr on the same day.

Post mortem findings concluded that the cause of death was cerebral oedema secondary to meningo-encephalitis. There was also a comment relating to the presence of both hyponatraemia and presumed inappropriate ADH secretion.

4. I have been asked to review her management, particularly with regard to fluid management and overall care. I have been asked to comment on any possible line of management that was below acceptable standards, and whether this contributes

to a significant breach of clinical duty. The Letter of Instruction includes a list of questions, and I shall respond to these in my report.

Clinical History

5. The next few paragraphs summarise Claire's clinical history. There is a past medical history of interest, and I include a brief chronology of this history.

6. Claire was born at full term. Her birth weight was 7lb 9 oz. The labour and delivery were reported as normal. There were no known problems in relation to her birth and no significant family history. Her mother and father were noted to be 26 and 28 years old at the time.

7. I have seen a detailed letter relating to Claire's hospital admission of 4.9.87. The letter is from Dr M Hanlon, paediatric registrar. Claire was 8 months of age at the time. She presented with a history of seizure activity. Short lasting seizures were noted on a number of occasions, and these continued following her discharge from hospital.

8. Electroencephalogram (EEG) dated 10.9.87 showed results that were outside the norm, with indefinite spike and slow wave. A repeat EEG (14 Sept 87) also sowed some irregularities, although these were not consistent with any specific phenomenon. A whole range of other investigations carried out at the time, including CT scan of the brain, failed to confirm any specific cause for her seizure activity. Claire was placed on anticonvulsant medication, which continued for many years.

9. I have no detailed information of Claire's development over the next few years. A letter dated 2 August 96 confirms that she has both learning disability and behaviour difficulties. There was no record of any seizure activity from the age of 4 years. She had been off anticonvulsant therapy (sodium valproate, *Epilim*) for the past year.

At the 1 August 96 clinic the issue of placing Claire on a therapeutic trial involving either Ritalin (methylphenidate) or placebo was discussed. She was prescribed Ritalin 10 mg daily.

Index event

10. Claire was admitted via the Accident and Emergency (A & E) Department at 8 pm on 21.10.96. The history was of vomiting at 3 pm and every hour since. There was also a history of *"slurred speech and drowsy"*. She had been unwell the previous day and there had been a history of loose motions three days earlier. Her father's Statement confirms that Claire had been at school that day (Monday).

The clinical entry confirms that under normal circumstances Claire's speech consisted of meaningful sentences and that her hearing and vision was normal. She was unable to dress herself. She could walk both up and downstairs. She favoured the left side of her body. She attended a local special school. The trial of Ritalin was noted and that it caused a dry mouth. It is not clear whether she was on Ritalin at this admission.

11. The initial clinical history is noted as follows. Her temperature was 37°C (normal). Pulse rate was 80 per minute. Examination of heart, chest and abdomen was normal. The neurological findings confirmed normal fundi. The discs were not blurred. She was noted to be sitting up and *"staring vacantly"*.
Reflexes were brisker on the right than the left. She was noted to be *"not responding to parents' voice / intermittently responding to deep pain."*

12. Claire was placed on a neurological monitoring system, and the results are noted here.

13. The diagnosis was suspected as being a viral illness. There was a second query regarding encephalitis, but this was crossed off. She was treated with intravenous fluids and diazepam, and a number of investigations were arranged.

14. Claire's investigations are included in the accompanied table.

15. The significant finding on admission was sodium of 132. The rest of the biochemistry was normal; in particular there was no evidence of significant dehydration.

s maintained on 0.18% sodium chloride ("fifth normal saline"). The ns that she was written up for 64 mln / hour. I enclose a copy of the his report.

a total 536 ml over 9 hours on 21 Oct (equivalent to 60 ml / hour), 07:00 hr the next day.
n 22 Oct until 02:00 hr on 23 Oct (just before she collapsed) she f 1,070 ml which works out at 53 ml/hr.
s several episodes of vomiting and of passing urine.

eived a neurology review at 4 pm on Tuesday 22 Oct. The clinical irmed that she did not have a raised temperature and there was no ngism. The neurological findings were as follows.

e opening to voice, non-verbal withdraws from painful stimulus.
ent right side?
r limbs.
tone both arms.
trically brisk.
ed both ankles.

en and looks vacantly.
mands.
qual, accommodation and reactive to light) *5 mm*
o papilloedema.
l lingual movements appear normal"

at the picture was of an acute encephalopathy, most probably post-reatment with phenytoin was suggested, with CT the following day if te up.

entry, written between 16:00 and 17:00 hr, notes *"still in status"* aning '*status* epilepticus'). She was therefore given midazolam 0.5 tely, followed by midazolam infusion 2 ug / kg / min, (which works irs).

I have seen a nursing entry in a sheet headed "Record of Attacks Observed". This notes: -

22/10	*"3.10 pm*	*Lasted frequently strong seizer* (sic) *at 3.25.*	*Duration 5 min*
	4.30	*Teeth tightened slightly*	*Few secs*
	7.15 pm	*Teeth clenched + groaned*	*1 min*
	9 pm	*Episode of screaming and drawing up of arms. Pulse rate 165 bpm. Pupils large but reacting to light. Dr informed"*	

I cannot find any other record of seizure activity in the file from this index event.

19. A further neurology review timed at 17:00 hr confirms that *"she continues to be largely unresponsive"*. A further history from her mother notes *"contact with cousin on Saturday who had a gastrointestinal upset. Claire had loose motions on Sunday and vomiting Monday. She had some focal signs on Monday with right sided stiffening"*.

Additional treatment with cefotaxime and acyclovir is advised. Viral cultures are checked and sodium valproate is prescribed; 20 mg/kg as IV bolus followed by 10 mg/kg over 12 hours.

The next entry is timed at 23:30 on 22 Oct. It notes sodium of 121, potassium 3.3, urea 2.9 and creatinine 33. There is a query regarding fluid overload with low sodium fluids and a further query regarding SIADH (syndrome of inappropriate antidiuretic hormone). Following discussions with the registrar her fluids are reduced to 2/3rds of their current volume; 41 ml/hr. Urine is checked for osmolality.

20. The entry timed at 3 am on 23 Oct notes
"Had been stable when suddenly she had a respiratory arrest and developed fixed dilated pupils". When seen she was showing Cheyne stokes (breathing) and receiving oxygen via face mask. The anaesthetist was called, intubated her orally with a 6.5 tube and transferred her to the PICU.

A review timed at 3 am (entry of 4 am) confirms that Claire is intubated and ventilated. Her pupils are noted to be fixed and dilated. There is bilateral papilloedema left more than right. Her blood pressure is 90/65, heart rate l00 / min. These values are acceptable.

Treatment was given with mannitol, dopamine infusion, and urgent CT scan arranged.

21. The entry timed at 05:30 hr is reported as showing results of the CT scan: there is severe diffuse hemispheric swelling with complete effacement of the basal systems, no focal abnormality is identified.

22. The entry timed at 6 am notes no response to stimulation. The clinical staff arrange brain stem tests. These are tests performed to check for brain viability in patients who are on life support, where recovery is deemed unlikely, and where life support may have to be discontinued.

23. There is an entry dated 23 Oct (untimed) noting that she now has polyuria, and that DDAVP (desmopressin, antidiuretic hormone, ADH) is required. Serum sodium is 129 (up from 121).

24. The entry timed at 18:25 hr notes that the diagnosis of brain death protocol is completed and that there is no spontaneous respiratory movement. Following discussion with the parents, ventilation is discontinued at 18:45 hr. Death is attributed to cerebral oedema secondary to status epilepticus.

25. I have seen the autopsy report from the RBHSC. It confirms that the time of death was 6.25 hr on 23.10.96. The report contains a clinical summary. The significant findings are as follows.

- Brain weight 1606 grams.
- Symmetrical brain swelling. On sectioning of the brain the presence of diffuse brain swelling is confirmed.
- Cortex and white matter sections show focal meningeal thickening and a cellular reaction in the meninges and perivascular space in the underlying cortex.
- There is no cortical necrosis but in the deep white matter focal collections of neurones are present arranged in a rather haphazard manner.
- Focal collection of neuoblasts in the subependymal zone suggestive of a migration problem.

The summary is as follows.

"The features are those of cerebral oedema with neuronal migrational defect and a low grade subacute meningo-encephalitis. No other discrete lesion has been identified to explain epileptic seizures. The reaction in the meninges and cortex is suggestive of a viral aetiology, though some viral studies were negative during life and on post mortem CSF.
With the clinical history of diarrhoea and vomiting there is a possibility though a metabolic cause cannot be entirely excluded. As this was a brain only autopsy it is not possible to comment on other systemic pathology in the general organs. No other structural lesion in the brain like corpus colosal or other malformations were identified."

26. I have seen the report of Dr Brian Harding consultant neuropathogist at Great Ormond Street Hospital, London (dated 22.8.07). He reports on the autopsy report of Dr Herron and on 32 H & E stained sections, 23 immunostained slides 4 semi thin slides and a further 13 H & E stained sections from various parts of the brain. His conclusions are as follows.

- There is no evidence of acquired infection (meningitis or encephalitis)
- The cause of death on the Death Certificate and in the Inquest verdict is not concordant with his observations.
- The brain weight is excessive (1606 grams). The normal weight is about 1200 grams (there is no record of Claire's head circumference to indicate whether head circumference was normal).

[I cannot find a record of head circumference from any of the clinical notes. DRE]

- "Effacement of gyri" and "uncal prominence" are rather weak indicators (of brain swelling). This is not supported by *"major downward shift of the brain and cerebellum which is common in severe swollen brain and by the microscopy (lack of vacuolation of white matter)."*
- He considers meningo-encephalitis excluded both by microbiology and the post mortem neuropathology.
- Hyponatraemia is known to cause brain swelling. But there is no other specific neuropathological indicator for hyponatraemia.

- Seizures were not witnessed prior to hospital admission, and certainly not status epilepticus.
- The neuropathological sequelea of status were not present.
- There was no damage to the hippocampus which may be seen in children with chronic epilepsy.

In Dr Harding's opinion the cause of death was brain swelling and, hyponatraemia is the only causative factor that has been positively identified.

27. Other investigations were carried out either following the death or where the results were obtained after Claire's death.

Cerebro-spinal fluid (CSF) analysis was obtained on 25.10.96. The results were received on 4.11.96. Clearly this fluid would have been obtained at post mortem. CSF is described as being blood stained and straw coloured. The protein content is 95.0 g/L. The normal reference range is 0.15 – 0.45.
CSF is noted to contain 300,000 red cells per ul and 4,000 leucocytes per ul. The leucocytes are described as being *"mostly lymphocytes"*. Subsequent CSF culture is reported as showing no growth in 48 hours (report of 28.10.96).

28. Serum samples looking for viruses, obtained on 21.10.96 is reported on 30.10.96 as showing negative findings for the following; mumps, measles, herpes simplex, herpes zoster (chicken pox) CMV, adenovirus, Q fever, PLGEV, mycoplasma pneumoniae and influenzae A and B. There is no record of any samples being sent off for viral culture, and no samples were sent off for PCR estimations.

29. The CT scan of the brain dated 23.10.96 is reported as follows.
"There is generalised cerebral swelling with effacement of the cortical sulci as well as the basal cisterns and the third ventricle. No focal lesion has been identied".

A chest x-ray of the same date is reported as showing *"patchy consolidation in the mid and upper zones on both sides, slightly more extensive in examination 2. An ETT* (endotracheal tube) *is in position with the tip at the thoracic inlet and in film 3 an IV line is present with the tip in the SVC* (superior vena cava)."
The presence of the ETT confirms that this chest x-ray was carried out following Claire's respiratory arrest.

I have not seen the original CT and chest x-ray.

30. For completion, I note the CSF findings from Claire's admission in September 1987. There were two samples dated 12.9.87. One sample was described as *"blood stained"*. Protein was 1.7 g/L. There were 8,400 red cells and less than I white cell. The second sample was described as being *"faintly blood stained"*. There were 1,140 red cells and less than I white cell. CSF culture was reported as showing no growth in 48 hours.

Opinion

31. My opinion is based on my experience as a consultant paediatrician in Swansea since 1980. The management of children who present with an altered level of consciousness is one that should be common to all practicing hospital based paediatricians. The presentation is one that should always be taken seriously. The cause is often not obvious, and one is always faced with the risk of the child deteriorating, falling into a coma, and sustaining a respiratory or cardio-respiratory arrest.

I have been involved with hospital based acute paediatrics throughout my career, from 1973 until the present day. The management of children with an altered level of consciousness is a clinical scenario I have encountered on numerous occasions during this time.

32. My first involvement with this case was following a consultation with two officers of the Northern Ireland Police Service on 24 Jan 08, and I am filing this report prior to a period of leave outside of the UK starting on 31 Jan 08. This report is a first draft, and I will add or amend my report on receipt of additional information.

33. My preliminary view is as follows. There does not appear to be any significant history relating to the pregnancy or birth. Claire was born at term. It looks as if her early development was appropriate.

34. Claire sustained a significant neurological illness at the age of 8 months. Tonic clonic convulsions were recorded on numerous occasions. The convulsions continued beyond her discharge, and she remained on anticonvulsant therapy until

the age of 4 years. The cause of this encephalopathic illness has never been ascertained. Investigations available at the time were not particularly helpful. Normal CSF would tend to rule out an infective cause. A normal CT scan of the brain does not help to establish a diagnosis. Electroencephalography (EEG) carried out at the time showed non-specific findings, not diagnostic of any specific disorder.

35. It looks as if the acute encephalopathic illness burnt itself out but left Claire with a residual permanent neuro-disability. A letter dated 9.2.88 from the consultant paediatrician at the Ulster Hospital records that Claire has had no convulsions since September (1987 presumably). She was on Epilim (sodium valproate) 2.7 ml twice daily at that time. The consultant notes that her speech is *"undoubtedly slow"*. She was also noted to grind her teeth, was able to sit well and get into the crawling position but doesn't really move forwards, but may go backwards. She is not standing with support. Claire was 13 months at that time.

There is a discrepancy in the documentation regarding the time that Claire had been seizure free. The letter from Dr Gaston of 30 May 96 notes that she has a history of seizures from 6 months to 4 years of age, and had been off Epilim for the past year. (presumably 1995). The entry from her index event suggests that the sodium valproate was discontinued at 4 years of age.

She experienced seizure activity for some time afterwards, but she had been free of seizures for many years prior to her index and final clinical presentation. She was left with learning difficulties. This is summarised in the letter of 30 May 96 when she was noted to have a short attention span, and features consistent with attention deficit disorder. All the documents suggest that Claire has had no history of seizures after 4 years of age.

Claire's index event

36. Claire was unwell for a very short period of time prior to her hospital admission on the evening of 21 Oct 1996. Her father's Statement notes that she attended school that day and that she had been sick before returning home at approximately 15:00 hr. The vomiting continued at home on 2 or 3 occasions. She also had one

loose bowel movement. Hospital admission was arranged following a visit from the GP at 18:00 hr.

37. There is nothing in Mr Roberts's Statement or in the medical notes to suggest that Claire has had any kind of convulsive episode. Right from the outset, the clinical entry describes very significant findings consistent with an altered level of consciousness. The initial entry of 8 pm records *"not responding to parents' voice / intermittently responding to deep pain".* There is therefore compelling evidence consistent with Claire having some kind of encephalopathic illness at presentation.

It is probably reasonable at this time to outline the likely cause of such a presentation, and the steps that would be taken by any medical practitioner to confirm or rule out any specific disorder, with the emphasis on confirming or ruling out any disorder that is treatable, and where early treatment can make a difference, and / or confirming or ruling out any disorder that is likely to lead to a deterioration.

38.

- There is no evidence of trauma; no head injury.

- Whilst one will get an altered level of consciousness following a seizure (and I used the word seizure, fit, convulsion or epileptic fit interchangeably) there is no evidence whatsoever of Claire having had a convulsion. She was under the supervision of adults; school teacher, parents, GP, continually in the hours leading to her hospital admission. The likelihood of her sustaining a convulsion without any one noticing is unrealistic in my opinion. Moreover, if her lack of response was a post-ictal phenomenon, one would expect the post-ictal phase to last several hours only in the event of a significant tonic clonic seizure (also known as a *grand mal* fit).

- There is no history of her having taken any medication or inappropriate drug. I am not quite certain whether she was on methylphenidate (Ritalin) at this time, but I would not expect methylphenidate to cause an event of this nature anyway.

39. Claire was not systemically ill, i.e. she did not have symptoms consistent with, for example, severe gastroenteritis sufficient to cause fluid loss and dehydration. She was not febrile. There was no clinical evidence to suggest a condition such as pneumonia or severe urinary tract infection. There was no clinical evidence of meningitis.

40. All the above conditions would have been ruled out as a matter of course during Claire's initial assessment. One is therefore left with a very worrying scenario, a child who has an altered level of consciousness and where the cause is not obvious. Whilst I would not be critical of anyone for not reaching a specific diagnosis at this time, her clinical presentation was sufficient to cause significant concern.

41. Having ruled out the above one is left with the very non-specific diagnosis, which is that of encephalopathy.

Encephalopathic illness is not uncommon in children. It frequently occurs as a complication of one of the viral illness such as measles, chickenpox or mumps. When associated with a specific infection the diagnosis is relatively straightforward, as one can find more common features of the disease. I suspect that my primary diagnosis would have been an encephalopathy secondary to an unknown viral infection. There was a history of vomiting and a mild tummy upset, and whilst one cannot explain the mechanism, certain viruses can cause this kind of presentation. Herpes simplex (which is the organism that causes cold sores) can cause encephalitis, so can enteroviruses. On admission therefore such an option would be at the top of my differential diagnosis.

42. Another diagnostic issue to consider is a so-called metabolic encephalopathy. I am responsible for the management of children with diabetes. A child who develops severe and protracted hypoglycaemia as a result of taking too much insulin or failure to take sufficient calories can develop a seizure, which would be followed by a period of altered consciousness. In serious cases this is associated with a degree of cerebral oedema. Indeed it may cause permanent neuronal damage. There is of course no evidence of such an event in Claire's case; I am using this example for illustrative purposes only.

Another disorder, more common during the 1970s and 80s, was Reye's syndrome. This is a very poorly understood disorder, which is thought to be linked to the prescribing of aspirin and / or some link with chickenpox. There are plenty of reports of Reye's Syndrome where there is no known aspirin or chicken pox contact. Children develop a liver disorder with an accompanying encephalopathy. It is disappointing that this disorder was not considered, and that there was a failure to arrange the necessary investigations, especially to check her liver enzymes and her serum ammonia level. Reye's syndrome is a serious disorder with a high mortality. Careful supportive therapy can make a significant difference.

43. I do not think that Claire had any of the rare inborn errors of metabolism, and which can create diagnostic confusion. Any such consideration is purely speculative, and I do not think that there is any purpose in exploring the matter in any detail.

44. I now turn to an interesting finding from the post mortem, and wish to raise this matter out of date order.

At post mortem the pathologist arranged analysis of the cerebral spinal fluid (CSF). The findings are interesting. The sample of CSF was unfortunately blood stained which makes interpretation more difficult. However the number of white cells (leucocytes) in the sample is far greater than what one would expect if the leucocytes reflected the normal "mix" of blood cells that had leaked into the CSF during the process of obtaining the CSF sample.

The CSF contained 300,000 RBCs and 4,000 leucocytes. This is a ratio of 1 : 75. I have looked at the results of Claire's blood tests during her admission. There were three, as follows.

21.10.96	RBC	3,760,000	white cells	16,520	ratio	I:228
23.10.96	RBC	3,660,000	white cells	9,350	ratio	I:391
23.10.96	RBC	3,860,000	white cells	5,540	ratio	I:696

Conventional teaching suggests that one should expect a ratio of 1 white cell (leucocyte) per 500 red cells if the blood found in a CSF sample has got there as a

result of the sampling process. In Claire's case, the red cell : white cell ratio ***in the blood*** ranges from 1:228 to 1 : 696, consistent with conventional teaching.

The CSF analysis in Claire's case contain disproportionate number of leucocytes, giving this low ratio; 1:75. This suggests that Claire's CSF contained a genuine increase in white cells, which is what one would find in a patient with meningo-encephalitis. It is also important to note that these white cells were *"mostly lymphocytes"*. This is what one would expect in a patient with a meningo-encephalitis of viral cause.

Normally, in the blood stream, there are two major types of white cell, neutrophils and lymphocytes. In an acute infection one gets a rapid rise in the neutrophil count. In a viral infection one may get an early increase in neutrophil count, but it is not uncommon to have a normal total number of white cells , or indeed a relative increase in lymphocyte count.

Unfortunately, there is no information regarding the type of white cell found in Claire's blood. The figure relates to the total white count only. I would predict that her first result (16,520 white cells) would have contained mainly neutrophils. The figure had dropped to 5,540 by 24 Oct. It is likely that by this time the numbers of neutrophils and lymphocytes would have been similar. This is the result where the red cell : white cell ratio is highest (1 : 696) . Whilst interpreting these findings is far from being an exact science, the difference in ratios between the blood sample of 24 Oct (1 : 696) and the ratio on the CSF sample obtained the following day (1:75) makes it quite probable that there were lymphocytes present in Claire's CSF, and that this is consistent with a diagnosis of viral meningo-encephalitis.

Observations on management

45. I have expressed my disappointment at the relative lack of investigations carried out early, particularly the failure to check Claire's plasma ammonia and her liver enzymes. Also, the medical care did not appear to have a "working diagnosis" or a "differential diagnosis" where one would list all possible options, if only to rule them out.

A "differential diagnosis" is a standard format used by all clinicians when working out the cause of a clinical disorder when the diagnosis is not immediately obvious. Interestingly, the handwritten entry comments on "viral infection". Encephalitis is also written down and is then crossed out. Clinically, I would be approaching the clinical management of Claire as a case of encephalopathy (and would not be particularly concerned if the term encephalopathy and encephalitis were used interchangeably. The former is a more generic descriptive term, whilst the term encephalitis indicates an infective disorder.)

46. The only investigations carried out soon after her admission were the basic ones, and my observations are as follows. Claire's haemoglobin was slightly low, and that is of no diagnostic help. Her white cell value (16,000) is raised. This is typical of an infection, but it does not distinguish the cause of the infection. I am rather surprised that a major children's hospital did not carry out a differential white count as a matter of course, providing information on the neutrophil count and lymphocyte count.

The medical officer queried the option of a lumbar puncture. This is the procedure carried out to obtain CSF, and is essential if one suspects meningitis. In the event, a lumbar puncture was not performed.

The only other investigation performed was the basic biochemistry. The key result is the sodium of 132. The laboratory's own reference range is 135 – 145. This range is quite wide. The key finding is that the sodium is low. Moreover the sodium is low in the presence of a normal potassium. The urea is normal at 4.5 (normal range 3.3 – 8.8). A normal urea suggests that Claire is not suffering any significant dehydration. I also note that the creatinine is at the lower end of the normal range at 36 (normal 40 – 110) but I am not sure that this is particularly useful as a pointer to confirming or ruling out any diagnosis.

The key result is the sodium of 132. It is low. Whilst a sodium of 132 is unlikely to cause any harm to a young child, within the context of Claire's clinical presentation it should be deemed to be of important diagnostic significance. It is not clear when the blood test was taken; I assume the test was taken soon after she was admitted to

hospital. The sodium of 132 is therefore indicative of her biochemical balance **prior to the introduction of any intravenous fluids.**

There was no evidence of significant dehydration, for the reasons I have described above. Her pulse rate was a satisfactory 80. One would expect a pulse rate of 100 or more in any child who was significantly dehydrated.

47. In my opinion, a sodium of 132 at or soon after hospital admission is evidence that Claire was already showing signs of retaining fluid. The lowish creatinine value probably indicates the same thing.
Within the context of her clinical condition; which is that she has an encephalopathy, one needs to consider seriously the possibility of her already experiencing the syndrome of inappropriate ADH (SIADH) secretion.

48. I enclose a summary of the pathophysiology and diagnosis of SIADH (Oski's Paediatrics, 2,206 – 7). Its consideration is essential to the safe management of any significantly ill child. The enclosed article contains a large list of disorders associated with this phenomenon. In clinical practice SIADH is most commonly associated with any severe systemic illness or a number of intracranial disorders such as head trauma, encephalitis or brain hypoxia. I shall comment on Claire's neurological observations later.

Intravenous fluid therapy

49. Claire weighed 24.1 kg. One calculates a child's fluid replacement as follows. One gives 100 ml / kg / 24 hours for the first 10 kg body weigh, 50 ml / kg per 24 hours for the next 10 kg body weight and 20 ml / kg per 24 hours for every subsequent kg body weight. A girl of 24 kg would therefore require a total of 1,000 + 500 + 80 ml per 24 hours, a total of 1,580 ml per 24 hr, or 65 ml / hr. One would give additional fluid in a patient who was dehydrated, but this was not relevant here.

Claire's fluid chart confirms that the fluid replacement therapy *was "5/N saline at 64 ml/hr"*. The rate of fluid is therefore correct. The intravenous fluid prescription chart notes 0.18% NaCl plus 4% Dextrose. Between 23:00 hr on 21 Oct and 07:00 hr the following morning Claire receives 536 ml. This averages 60 ml / hr over 9 hours. The fluid chart also records seven separate episodes of vomit during this time.

50. I enclose a copy of the chapter on Fluid and Electrolyte Management from the "Advanced Paediatric Life Support" manual. The second edition was published in 1997. Whilst there is no controversy regarding the volume of fluid required, there is concern in paediatric circles regarding the type of fluid that should be prescribed. 0.18% sodium chloride with added glucose has been a commonly used fluid in paediatric practice and the 1997 edition continues to recommend it as a standard regime (page 249). It has been my practice to insist on the use of 0.45% NaCl as the standard fluid therapy for sick children, and cannot recall a time when I was comfortable with using 0.18% solution. I have always been concerned about the risk "waterlogging" a patient by giving too dilute a solution. That is, running the risk of a patient becoming oedematous (fluid overload) and sustaining a consequent drop in serum sodium. Whilst I would have prescribed 0.45% Dextrose from the onset I have to acknowledge that, by 1996 standards, 0.18% solution remained a recommended regime in the published literature.

51. This takes me to my next observation, which is whether prescribing 0.18% NaCl was appropriate ***in this patient at this time***. In my opinion once it was known that Claire's sodium was 132 her fluid regime should have changed immediately to 0.45% NaCl. The fluid chart notes that intravenous therapy was only commenced at about 23:00 hr, so it is virtually certain that the value of 132 pre dates intravenous therapy i.e. Claire is showing evidence of fluid retention ***prior to receiving intravenous fluids***. In conjunction with her clinical encephalopathy, there is compelling grounds for considering a diagnosis of SIADH already.

I have commented earlier on the possibility of Reye's syndrome, and whilst there is insufficient evidence to confirm the diagnosis, the continued history of vomit is not atypical. The vomiting could also of course be a reflection of Claire now developing a gradual increase in intracranial pressure.

52. The fluid chart does not record Claire receiving any oral fluid from the time of admission, other than sips of water. One would therefore expect any history of vomiting to reduce both in volume and in frequency. The chart for the following day, from 08:00 onwards, does not record any further vomiting until two separate entries

at midnight and 01:00 hr (a couple of hours before she collapsed) where she is noted to have brought up *"small mouthfuls"*.

53. The fluid chart notes that Claire has passed urine (PU) at 03:00 hr, 11:00 hr, 19:00 hr and 21:00 hr during Tuesday 22 Oct. The volume of urine is not recorded. The nursing entry records *"urinary catheter inserted 22.10.96"*. Time of insertion is not recorded. The entry is from the paediatric intensive care unit so I presume this occurred following her respiratory arrest (in the early hours of 23 Oct.

54. The nursing entry timed at 10 pm on the night of admission confirms *"two small bile stained vomits"*. A further bile stained vomit is recorded at 7 am.

55. There is no record of urinary volume and there is no evidence of any urine analysis (apart from one test looking for evidence of infection). There is therefore no information regarding urine concentration or urinary sodium or osmolality. These investigations can be carried out routinely, and results obtained quickly.

If Claire was passing urine voluntarily, measuring urine volume is straight forward, and assessing its concentration (osmolality) and sodium output should be a routine procedure. This is noted in the APLS protocol. If Claire's level of consciousness was associated with incontinence urinary catheter should have been performed as a routine procedure. Failure to conduct these measurements is indicative of unsatisfactory clinical practice. It was also unsatisfactory not to carry out a repeat blood electrolyte investigation (to monitor sodium, potassium , urea, creatinine and serum osmolality) on the morning following her admission. It is virtually certain that her sodium value would have fallen below 132, and any results below 130 would have alerted any medical practitioner to the possibility indeed probability of inappropriate fluid retention irrespective of whether this was part of the phenomenon of SIADH. The lower sodium would also have alerted any reasonable medical practitioner to the need to monitor urinary output obsessionally, and arrange the investigations described above.

In the event Claire's fluid management was not changed at all. I have already noted that she should have been placed on 0.45% NaCl as of midnight on the night of admission (when the sodium result returned at 132). I would have added potassium

chloride (KCl) to her fluid regime from the outset. Her potassium level fell, although the failure to use KCl probably did not influence outcome, and I won't comment on this aspect of her care any further.

Claire was maintained on the same volume of fluid replacement throughout Tuesday 22 Oct. If the medical staff had repeated the blood serum sodium and monitoring urinary sodium they would have had the option of adjusting fluid regime carefully and accurately. Increased sodium in the urine would have confirmed the diagnosis of SIADH, allowing treatment with a combination of adjusting fluid volume and prescribing a more concentrated sodium chloride solution. Getting the fluid balance right can be extremely tricky, and it would not be possible to describe in detail Claire's ideal fluid replacement; it would depend on regular monitoring of both serum and urinary sodium levels, and of course on her overall condition.

The other advantage of course of considering SIADH as part of Claire's condition is that it would strengthen the clinical impression of an encephalopathy.

56. I have seen the central nervous system (CNS) observation chart. It was only commenced at I pm on the day following admission. For the record, she should have been on a CNS observation chart (on "neuro obs") from her admission. *"Not responding to parents' voice"* and *"intermittently responding to deep pain"* are both indicators of a serious neurological disorder. Failure to place Claire on a CNS observation chart is indicative of unsatisfactory care.

The chart records the Glasgow Coma Scale (GCS). The results are extremely disturbing, more or less from 1 pm, where the score is 9. From 4 pm her response is limited to the ability to localise pain. Her pulse rate, blood pressure and respiratory rate remained pretty stable throughout.

The only information regarding possible seizure activity is the nursing entry timed at 3.15 pm on 22 Oct. In my opinion these symptoms reflect her worsening condition. Her Coma Chart was getting worse about the same time. The presumed seizure was a reflection, probably, of increased intracranial pressure, ie, a reflection of (relatively) early cerebral oedema. Given the absence of obvious seizure activity at admission,

and during the next few hours, I do not think that this episode reflects primary epilepsy (or status epilepticus).

57. In my opinion Claire should have had an urgent CT scan on the day following her admission. Indeed there were grounds for demanding a scan first thing in the morning. She had shown significant altered level of consciousness of nearly 12 hours by 9 am the following day; she was showing no sign of improvement, there was no obvious evidence of infection, and there were minor but significant biochemical abnormalities (sodium of 132) recorded from the previous evening. In my opinion failing to demand CT scan during Tuesday 22nd October is indicative of unsatisfactory care. The result is likely to have shown some evidence of cerebral oedema, allowing intervention with mannitol, plus accurate manipulation of intravenous fluid. One would also have the option of considering transfer to a high dependency area. I suspect that the hospital has a neurosurgery department, and there would be the option of considering intracranial pressure monitoring as well. Effective and frequent monitoring of both fluid intake and urinary output, plus intervention with mannitol if there was evidence of cerebral oedema on an earlier CT scan, could have led to a reversal of her symptoms, avoiding the catastrophe that she experienced in the early hours of the following day.

The issue of status epilepticus

58. The working diagnosis, at least from the 22nd Oct was "*non fitting status*", meaning status epilepticus. I disagree. The concept of *"non fitting status epilepticus"* is rather nebulous anyway, although I would recognise that such a phenomenon may occur, but typically in children who have a well documented history of epilepsy, usually difficult to control. Claire had experienced no seizures for years, and there is nothing in her history to suggest that she had any kind of seizure prior to admission or later. I would not have prescribed phenytoin, although I don't think that the phenytoin contributed to her demise in any way. I would not have prescribed midazolam. The problem with this drug is that it would have significantly altered her level of consciousness, confusing the natural picture.

If one makes the **hypothetical** assumption that Claire was experiencing status epilepticus it does not detract from the concerns and criticisms that I have regarding

the failure to monitor her blood and urine frequently and the failure to organise CT scanning. After all, if Claire was experiencing status epilepticus (and I don't think she was) her condition was even more serious, and the need to arrange the above investigations was even more pressing.

The post mortem findings

59. I cannot possibly comment where two pathologists have prepared reports that have different conclusions. Neither has commented on the results of the post mortem CSF, and whilst I am comfortable with the interpretation described above, I need to add the caveat which is that I am not familiar with commenting on CSF analysis carried out after death. As far as I know, there would be no significant post mortem changes, although I would defer to a pathology or neuropathology opinion on this particular aspect of the case.

Summary

60. Claire was a young girl of 9 years who had a history of learning difficulties, probably following a serious neurological illness at the age of 8 months.

61. Claire presented to hospital with a relatively short history of vomiting and loose stools. She had been well enough to go to school on the day of her admission.

62. Her clinical condition showed a significant altered level of consciousness from her arrival in hospital. In the absence of a history of seizure activity, head trauma, or accidental drug ingestion, an encephalopathic illness should have been considered on the night of admission. I would not be critical of the failure to identify the specific cause of the encephalopathy.

63. Given her altered level of consciousness and a history of vomiting in a previously physically well child, investigations should have included tests to rule out Reye's syndrome. These would have included checking her liver enzymes, blood ammonia and prothrombin time. Reye's syndrome is a possible diagnosis, but it cannot be confirmed, given the failure to carry out the above tests, and the unavailability of liver tissue for post mortem examination.

64. The initial volume of intravenous fluid prescribed is consistent with current protocols. Whilst the use of 0.18% NaCl as fluid replacement therapy is one of the options available in the protocols of the time, the fluid should have been replaced by stronger concentration, in the form of 0.45% NaCl, as of midnight (when the biochemistry results showed a sodium value of 132).

65. A combination of clinical encephalopathy and low serum sodium should alert any medical practitioner to the possibility of SAIDH as an additional complication.

66. Irrespective of the significance of SAIDH, failure to change fluid to 0.45%, and the failure to monitor both the urine volume and also urine concentration and urinary sodium is indicative of a level of care that is below acceptable standards in a modern children's department in the British Isles during the 1990s. Accurate and frequent measurement of both serum and urine sodium values would have allowed careful attention to Claire's fluid balance, minimising the risk of cerebral oedema.

67. Failure to arrange CT scan at any time on the day following her admission is indicative of a level of care that falls significantly below acceptable standards in a modern children's department in the British Isles. There was compelling evidence of an encephalopathic illness for which there was no clear explanation. Her condition showed no sign of improving during the day; the CNS observation chart showed a deterioration throughout the day.

Failure to place Claire on a CNS observation chart from her time of admission is also indicative of an unsatisfactory level of care by the standards of a modern children's department in the British Isles during the 1990s.

68. Careful monitoring of Claire's fluid balance, and arranging earlier CT scan would have alerted medical staff to the earlier diagnosis of cerebral oedema. Earlier intervention, by means of mannitol, supported by the option of intensive monitoring in a children's intensive care unit, could have held up the progression of the cerebral oedema, reversed its effect, and prevented the respiratory arrest.

69. The cause of Claire's encephalopathy must remain speculative, in view of the difference of opinion of the two pathologists. The prodomal history of vomiting and

loose stool, in association with the raised blood white cells at presentation, and the presence of an apparent increased number of lymphocytes in the post mortem CSF is consistent with a clinical diagnosis of meningo-encephalitis. The histological findings of the local pathologist are consistent with the clinical impression. The findings of the second pathologist does not support that diagnosis. I cannot possibly comment on the different interpretation of the two pathologists. I would advise that one obtains an additional opinion from Drs Herron and Harding, seeking their views on the post-mortem CSF findings, and whether the presence of 5,000 leucocytes (in a sample containing 300,000 red cells) is sufficient to warrant a diagnosis of meningo-encephalitis.

70. There is no evidence in my opinion of Claire having had a seizure or that her condition was due to status epilepticus. The episode described at 3.15 pm on 22 Oct (my paragraph 18) was an indication of her worsening neurological condition, not the cause of it.

71. I am certain that the direct cause of death was cerebral oedema, and that the hyponatraemia was due initially to the syndrome of inappropriate ADH. The progression of the hyponatraemia was due to the failure to prescribe the appropriate fluid and the failure to take adequate measures to monitor sodium balance and the consequent failure to change both the type of fluid given and its volume. The failure was exacerbated by the delay in organising CT scanning, which led to the delay in identifying cerebral oedema.

72. There was no reasonable hope of recovery once Claire experienced her respiratory arrest during the early hours of Wednesday 23 Oct, when she sustained her respiratory arrest and was found to have fixed dilated pupils.

2008/Roberts/N.48

Re: Claire Roberts dob 10.1.87 died 23.l0.96