CONFIDENTIAL REPORT

CLAIRE ROBERTS

The final illness of Claire Roberts culminating in her admission from 21st-23rd October 1996, when she died aged 9 years and 9 months, occurred from the background of unexplained severe cognitive impairment and epilepsy but this latter was in remission and she was not receiving anti-epilepsy medication – in fact, no medication at all.

The early symptoms of malaise, vomiting, drowsiness and slurred speech had led to the diagnosis of an inter-current virus illness and the investigation and post mortem findings only added acute cerebral oedema to the diagnosis, but not its cause. Thus we have no clear cause for this acute illness and a probable virus infection is a reasonable suggestion. Dr Webb advised that sub-clinical epilepsy was a likely mechanism for her deterioration. This was on the basis of previous epilepsy and a history of a small number of recent seizures obtained from members of her family and an observed seizure. On the basis of this diagnosis she was treated with rectal diazepam, IV phenytoin (an overdose), midazolam and sodium valproate in the face of a fluctuating but decreasing conscious level (i.e, dropping Glasgow Coma Scores).

Although there is mention of performing an EEG the following day, I am surprised that one was not performed urgently at the time when I.V phenytoin was contemplated to confirm the diagnosis of a high rate of sub-clinical epileptic seizure activity. I also think that sub-clinical seizure activity is an unlikely cause of this clinical presentation in someone who is in remission from her epilepsy, but not impossible. EEG is a simple test to confirm whether or not there is sub-clinical seizure activity. In Claire's case, it was assumed that she had sub-clinical seizure activity and this was treated aggressively. No one appears to have looked for an alternative treatable condition until she was admitted to ICU on 23rd October 1996 and was noted to have fixed dilated pupils and papilloedema.

Claire's earlier seizures as a baby raised the issue that she could be suffering from recurring seizures in October 1996. This was fair. The fact that a consultant neurologist was consulted for advice possibly led down the line of focussing on potential neurological problems, but would not have meant that the clinicians would have focussed solely on seizures and is not an excuse for failing to consider other matters.

I would not have described Claire as currently a person with epilepsy before her final illness. She was a child with a history of epilepsy which was in remission. It was more likely for her to have seizures / epilepsy in October 1996 than a child who had no such history because she had previously suffered from seizures / epilepsy.

It is more likely that hyponatraemia and brain oedema caused the seizures on 22nd October from 15.10 / 15.25 onwards and the reduced conscious level because non-convulsive epilepsy causes reduced and often fluctuating conscious levels Her condition was probably irretrievable by the time of the CT scan showing severe cerebral oedema.

The hyponatraemia (mild on presentation and marked when repeated) would have contributed in a major way to her cerebral oedema. It is difficult on the data available to be sure of the relative contributions to the cerebral oedema of:

- the original illness, whatever it was
- giving hypotonic fluids
- inappropriate antidiuretic hormone secretion as a result of the neurological illness.

However it is clear that the possibility of hyponatraemia / cerebral oedema was not considered until it was too late.

To my mind the errors were as follows:

- attributing deterioration to uncorroborated sub-clinical seizure activity.

- not recognising that the slight initial hyponatraemia might be part of a worsening trajectory and thus not realising that hypotonic fluids might be hazardous but certainly taking the lowered GCS/CNS observations which commenced at 13.00 on 22nd October 1996 as needing explanation by urgent scan, EEG and plasma sodium level in order to exclude non-convulsive status epilepticus and confirm progressive hyponatraemia and the presence of cerebral oedema, this latter condition being potentially fatal, but one for which there are treatments. The management of cerebral oedema using IV mannitol, fluid restriction and ventilation to keep the partial pressure of carbon dioxide (PCO_2) to a mildly sub-physiological level, which is a commonly used method of lowering intracranial pressure, was not performed until it was too late. Though the normal range of PCO2 for a child of Claire's age is 35-50mmHg. her partial pressure of carbon dioxide could have been maintained at 25-30mmHg (which is slightly lower than normal) to reduce intracranial pressure. Ventilation at this level operates by vasoconstriction i.e. restricting the blood vessels thereby reducing the blood in the head. Elective ventilation can only be done in PICU. Claire's reading of 79.2 in PICU (Ref: 090-022-059) was high and indicated underventilation, a possibly lower conscious level and the possibility of raised intracranial pressure. CNS observations should have been commenced and admission to the High Dependency Unit should have been considered from the ward round on 22nd October 1996.

I recognise that without a primary diagnosis and only a marginally lowered sodium level this was not an easy sequence to predict, but, with the deterioration in consciousness, I think there was a lack of urgency about investigating the reasons for this and thus a delay in any intervention. Non-convulsive status epilepticus is easy to confirm or exclude by EEG.

An EEG is the only method of confirming a diagnosis of non- convulsive status epilepticus. A CT scan cannot confirm this. In the context of an acute illness with reduced conscious level, a CT scan can show haemorrhage, hydrocephalus, cerebral oedema, but not subtle conditions. A MRI would show more detail than a CT scan and would be more likely to show subtle conditions. For the purposes for which they were carrying out a CT scan in Claire's case, a CT scan was adequate to identify most acute and treatable problems - but was performed very late. If the result had been unclear or inconclusive, then an MRI scan should have been carried out.

The problem with cerebral oedema is that the brain / skull accommodates increased fluid up to a point and then the pressure rises in the head and the blood supply to the brain is restricted. For this reason many units monitor intracranial pressure in this situation. This is by a neurosurgeon inserting a pressure monitor device subdurally or intra-ventricularly and was accepted as a method of monitoring but was not routine practice in October 1996. It is unfortunate that sub-clinical epilepsy was given precedence over raised intracranial pressure in terms of clinical management. However I am not suggesting that intracranial pressure monitoring should definitely have been used.

As for the primary diagnosis in Claire this remains unknown. One pathologist reported some abnormal findings in brain development. However I think that Dr Brian Harding's conclusion of "no cerebral malformation" should be taken because of his very great experience of this branch of paediatric neuropathology. The absence of a specific underlying causative diagnosis from the autopsy would not be unusual. SIADH (syndrome of inappropriate antidiuretic hormone hypersecretion) is a risk for any child with a neurological disease who becomes ill and intercurrent virus infection is the most likely in my view.

Turning to the specific questions:

(i) The appropriateness of the decision to admit Claire under the care of a consultant paediatrician rather than a consultant paediatric neurologist.

Entirely appropriate. It would be very unusual to go from A&E to a paediatric neurologist.

(ii) The quality of the diagnostic assessment and management by the paediatric registrar, Dr Bernie O'Hare, on admission on 21st October 1996, including:

Competent examination

(a) The differential diagnosis that a reasonably competent Paediatric Registrar would have made, given the information available to him / her at the time of Claire's admission to the ward.

The differential diagnosis omitted hyponatraemia / cerebral oedema and blood electrolytes were performed but a scan was not. The appropriate scan in this situation would have been an MRI but CTs were still being done instead in this situation in UK centres and should have shown oedema if performed earlier. Thus a CT was adequate to exclude or confirm a number of causes of raised intracranial pressure as the cause of reduced consciousness but MRI might have been needed if negative. A MRI scan would have been advisable if the CT scan was either unclear or inconclusive.

The differential diagnosis would have included: (1) Encephalitis. (2) Overwhelming infection. (3) Metabolic disorders including acute liver failure / hyponatraemia with cerebral oedema. (4) Intracranial haemorrhage. (5) Hydrocephalus. (6) Poisoning. (7) Non-convulsive status epilepticus.

I would have expected a paediatric registrar to have suggested 1,2,3,4 and 6 but might not be aware of 5 or 7.

I think that hyponatraemia / cerebral oedema should have been thought of and tested for in a child with vomiting and reduced consciousness in A&E and onwards, i.e.

- On Claire's attendance at A&E on 21 October 1996
- On admission to Allen ward, RBHSC
- On receipt of the serum sodium result of 132mmol/l at or after midnight on 22 October 1996
- At the ward round on 22 October 1996
- When Dr. Webb first saw Claire on 22 October 1996 at about 14.00h.

Dr O'Hare's examination was adequate but the differential diagnosis and investigations were not but would normally have been discussed with the Consultant.

(b) Whether the investigations proposed were appropriate and sufficiently comprehensively in the circumstances, and if not, why they were not.

The blood tests in my view should have included liver function tests and a toxic screen (the latter might have been deferred until the first blood tests returned and there was a

scan result). An MRI or CT would have been an urgent requirement and EEG ordered if no diagnosis emerged from that and the blood tests to assist with the possibility of encephalitis or non-convulsive status epilepticus.

A CT scan ought to have been carried out on the evening of 21st October 1996. If the emergency CT scanner was in the adult hospital, then that is where the child should have gone for the test. It was likely there was only 1 CT scanner. Nowadays a CT scan can be called up on a computer as soon as it is done. In 1996, a consultant neurologist would either have gone to see the scan being done or phoned the radiologist to discover what the CT scan showed.

I think that the CT scan was required urgently on the basis of a child having unexplained reduced consciousness. I would expect a Paediatric Registrar to discuss this patient with the Consultant Paediatrician and whatever the rules about who has to agree a scan, it should have been performed that night.

In the case of encephalitis, the waves may be slower than they ought to be and sometimes there is a higher voltage in the part of the brain affected by the inflammatory reaction. An EEG might detect the higher voltage and slower rate of waves e.g. focal slow wave abnormality or generalised slow wave abnormality.

(c) The appropriateness, in the circumstances, of the prescription at admission for IV fluid therapy, including:

- **Whether both the nature and the volume of the IV fluid prescribed was within the usually accepted practice at the time.**
- **Whether both the nature and the volume of the IV fluid prescribed would be appropriate now, and if not, what the appropriate fluid regime would be.**
- **Whether, in the light of Claire's condition, additional consideration should have been given to a more restricted fluid regime than that prescribed.**

On Claire's admission, many would have administered IV fluids of either 0.45% or 0.9% saline as a precautionary measure. The use of 0.18N saline in a drowsy child should have been with at least a warning for urgent review and it would be appropriate to use restricted fluids (i.e. 1000ml/M^2 / day) and many would use a higher NaCl concentration containing fluid. I think that a higher concentration of salt containing fluid regime should have been used when initial low sodium level came back at midnight. The management with 0.18N NaCl I have commented on as being potentially unwise but certainly requiring careful monitoring of consciousness and of the sodium level in the plasma.

When the first serum sodium concentration result returned at approximately midnight on 22nd October 1996, either 0.45% or 0.9% saline should have been administered as a precautionary measure (although not everyone would have done so), plus a repeat test of the serum sodium concentration should have been carried out. The problem was there was no repeat serum sodium test 6 hours from the first test.

(iii) The frequency of blood and electrolyte results, including:

(a) Whether the blood results (from the sample obtained on 21st October 1996) received after midnight on 22nd October 1996 were abnormal in any way and whether they mandated a reassessment and / or any change in management.

The sodium level of 132 was just below the normal range and needed to be urgently repeated and fluid regime altered to restrict fluids 1000ml/m^2/24hrs and given as N saline until it is clear that the sodium is not dropping to levels that would cause cerebral oedema.

(b) The appropriate time(s), with your reasons, that Claire's electrolyte should have been checked, given the IV therapy and that her serum sodium was 132mmol/L after midnight on 22nd October 1996.

Certainly the electrolytes should have been urgently repeated 6 hours after admission because of the reduced conscious level and the marginally reduced initial sodium level. I do not think it was reasonable to wait longer in this clinical situation, whatever the arrangements for biochemistry at night.

(iv) The quality of Dr Sands' diagnostic assessment and management of Claire, including:

(a) The reasonableness or otherwise of Dr Sands' diagnosis of non-convulsive status epilepticus the following morning (on 22nd October 1996) and of the other recorded differentials of encephalitis and encephalopathy, including:

- **The evidence on which your opinion is based.**
- **Whether any other conditions should have been considered in Dr Sands' differential diagnosis at that time and if so why.**

I would not agree that non-convulsive status epilepticus was the likely diagnosis because it is not common and epilepsy was not prominent in this girl's recent history. In my opinion non-convulsive status epilepticus needed to be proved by an urgent EEG. Another more likely cause of reduced conscious level and poorly reacting pupils would be cerebral oedema related to hyponatraemia and that should have been considered as a matter of urgency because in its early stages it is reversible by treatment.

The differential diagnosis that I think should have been considered by Dr Sands I have given earlier with what a paediatric registrar might be expected to know. It contains

1) *Encephalitis: which was considered by Dr Sands, i.e. an inflammatory brain disease caused by an infecting agent, usually a virus or by an allergic / autoimmune process. Encephalopathy is merely an all encompassing word for any brain illness that disturbs consciousness and includes most of what I have written but is not a diagnosis as such.

2) Overwhelming infection: usually bacterial, which would have been accompanied by low blood pressure and I would accept that there was no positive sign of infection and the specific neurological features would not usually occur. The reason for considering it is because it is treatable.

3) *Metabolic disorders: a combination of encephalopathy with acute liver disease (Reye's syndrome) is uncommon but readily excluded by liver function (blood) tests and would modify treatment.

4) Hyponatraemia / cerebral oedema is much more likely and this is discussed, including its treatability in this document. This can also co-exist with other brain illnesses.

5) *Intracranial haemorrhage: which may be spontaneous or caused by trauma may be treatable neurosurgically.

6) Hydrocephalus may present late but is very unlikely in view of the lack of evidence on an earlier scan. (Both 4 and 5 are readily excluded by either CT or MRI.)

7) *Poisoning: as a cause of unexplained consciousness and abnormal neurological state should be considered. The fluctuation in her condition makes this unlikely however.

8) Non-convulsive status epilepticus – discussed elsewhere in this document.

*These are the diagnoses that I think should have been within the competence of a paediatric registrar.

(b) The appropriateness or otherwise of Dr Sands' treatment using rectal Diazepam.

The problem with the diagnosis of non-convulsive status is that it leads to inappropriate treatment with anti-epilepsy drugs which could have further reduced her conscious level and her respiratory drive. If a single dose of rectal diazepam was to be given it should have been backed up by an urgent EEG, so that the working diagnosis could have been confirmed or refuted before any further anti-epilepsy medication was given. I think giving one dose of diazepam was reasonable in this situation.

- **Whether it was competent practice in October 1996 to use anti-epilepsy drugs without first having obtained an EEG**

  I have said that one dose of diazepam would be understandable but not more than this or the rest of the IV drugs without EEG, at least a CT scan and checking the electrolytes (i.e Na).

- **Whether it was competent practice in October 1996 to use anti-epilepsy drugs without having made further attempts to rule out primary hyponatraemia by rechecking her blood electrolytes**

  No, I think this should have been done.

(c) The reasonableness of the referral by Dr Sands to Dr Webb, consultant paediatric neurologist, who saw Claire at either 1400h or 1600h (depending on whether his recall, or the time appended to the case notes, is correct) including:

The lack of an urgent EEG, CT and electrolytes were major omissions and the need for these would normally have been discussed with a consultant. The reasons for these investigations are:

- The EEG to confirm or exclude non-convulsive status epilepticus.

- The CT was to exclude a space occupying lesion, particularly haemorrhage and to confirm cerebral oedema.

- Electrolytes were to plot the trend of the sodium level and to modify management if it had dropped further.

The CT scan and EEG should have been arranged at the latest by the morning of 22nd October 1996.

The consultant for such a discussion would normally be the designated paediatrician who would decide if a neurological opinion is required.

Dr. Steen should have agreed the referral to Dr. Webb. She would have known the strengths / weaknesses of the doctor [Dr. Sands or the SHO] to whom she was talking. The referral for neurology advice was appropriate, whether or not it was arranged in the proper way by Dr. Sands.

If a paediatric neurologist (Dr Webb) is available on site, I do not know if the paediatric registrars had permission to go directly to him but either way this referral was appropriate.

It would however be normal practice for the consultant paediatrician to ask for a neurological opinion so that they are kept fully informed about a patient under their care.

It is necessary to know the practice in the unit in relation to transfer of a patient to another consultant. It appears from the documents that Dr. Steen and the medical team retained primary care of Claire whilst seeking specialist advice from Dr. Webb. In that case, a junior member of staff would commonly see the patient and also show the patient to the consultant neurologist, the consultant neurologist would see the patient, write in the medical notes and indicate that s/he was available for further discussion, and if the neurologist felt the situation to be grave, s/he would normally speak directly to the paediatric consultant. If Dr. Steen was looking after Claire, she should have seen her on 22nd October 1996 and followed up on Dr. Webb's attendances. I would have expected Dr. Steen to have seen Claire before Dr. Webb attended at approximately 14.00, because the findings of Dr. Sands on the ward round would have required her to attend.

(d) Whether it was reasonable for Dr Webb not to have seen Claire until 14.00h or 16.00h

This is very difficult – usually in the UK a paediatric neurologist is in another hospital and advice is sought by telephone and / or agreed transfer. If Dr Webb was the "gatekeeper" for CT scans then he should have been asked earlier but otherwise this sort of delay could occur in other units.

(e) Whether Dr Steen, the consultant paediatrician under whom Claire had been admitted should have been informed, or been asked to attend, prior to Dr Webb's arrival.

In my view the cause of Claire's brain illness was unexplained and the consultant should have been involved. Whether this would usually happen in this unit I cannot say so that the onus of making it happen could be with the registrar / consultant or both.

(f) The appropriateness of the continuing IV fluid therapy, including:

Although 0.18 N saline was in common use, in the context of a low sodium level and reduced consciousness, it would have been more appropriate to give a reduced volume

of a higher strength of sodium chloride and to carefully monitor the sodium level in the plasma and the conscious level.

Claire's fluid management ought to have been reviewed throughout 22nd October given her deteriorating level of consciousness/drop in GCS scores/CNS observations (Ref:090-039-137), the "attacks" as recorded at Ref: 090-042-144, the lack of response to 4 types of anti-epileptic medication on 22nd October 1996 and the lack of urine output between 11.00 and 19.00 on 22nd October 1996.

- **Whether both the nature and the volume of the IV fluid prescribed was within the usually accepted practice at the time.**

  What was given was routine, but should have been carefully monitored in these circumstances.

- **Whether both the nature and the volume of the IV fluid prescribed would be appropriate now, and if not, what the appropriate fluid regime would be.**

  Now I think a higher sodium concentration and fluid restriction would be routine until it was clear what was happening to plasma sodium levels at conscious level and a brain scan had been performed.

(v) The quality of the diagnostic assessment and management by Dr Webb when he saw Claire on the afternoon of 22nd October 1996, including:

Dr Webb's assessment on the afternoon of 22nd October 1996 was a competent examination but the interpretation failed to include the possibility of rising intracranial pressure to explain her reduced conscious level and motor signs. I have given the differential diagnosis that I think should have been used.

Neurological examination was carried out on admission and on ward round. Dr. Webb carried out a neurological examination on his first attendance and recorded this in the notes. Thereafter he likely carried out a neurological examination/assessment on his 2nd and 3rd attendances but only recorded the positive findings or important negative findings. A neurological examination is not necessary after a seizure, but should be carried out when there is a drop in GCS score.

(a) The accuracy or otherwise of his note that Claire had a "(N) biochemistry profile ...." (Ref: 090-022-054), given that she had a sodium result of 132mmol/L, which was from a sample obtained the previous night.

(b) Whether any action should have been taken in regard to Claire's biochemical status at the time.

The sodium level of 132 mmol/l was just below the lower limit of the reference range and although not grossly abnormal should have prompted urgent repeat levels and management which would have been appropriate for a falling sodium level.

I have stated that 6 hours after the first blood test the electrolytes should have been repeated – this was before Dr Webb was involved but he should have required an urgent Na level as part of his assessment because of the likely possibility of falling Na levels, cerebral oedema and a fatal outcome which might be preventable by treatment with fluid restriction and higher sodium containing fluids, diuretics and hyperventilation.

(c) Whether the apparent error in the calculation of the prescription for phenytoin given by the SHO on Dr Webb's instructions would have had any ill effect.

I do not think that giving I.V. phenytoin was appropriate at that stage without proof that non-convulsive status epilepticus was present. A significant overdose is unfortunate, but I do not think it is likely to have materially altered the outcome, although it is a feature of the pharmaco-dynamics of giving phenytoin that above a certain dose the phenytoin blood level rises faster than for the same dose at lower doses and thus one more easily gets to toxic levels. I am not sure however that this adds much that is useful.

- **Please explain the effect upon Claire of being administered a loading dose of 635mg of Phenytoin at 14.45 (Ref: 090-026-075), rather than 432mg, particularly in terms of her level of consciousness and general condition.**

  It could reduce her conscious level temporarily and increase the chance of cardiac side effects but the latter did not occur. The overdose of 635 mg (rather than 432mg) of phenytoin administered at 14.45 (Ref: 090-026-075) was not a huge overdose. It is possible that it contributed to this fall in Claire's GCS at 15.00, but this is not definite. However it is unlikely that it caused the drop in her GCS score at 16.00 and 17.00.

- **Please comment upon the extent to which the effect on Claire's presentation of such an overdose could have affected the diagnosis of her condition.**

  It might have reduced conscious level but I don't think that this is likely to have had a major effect on diagnosis or management. There is a recent recommendation that the dose given should be 20mg/kg because of problems in calculating the dose.

(d) The continuing anticonvulsant therapy arranged by Dr Webb and in particular:-

- **At 1400/1600**
- **Between 1430 and 1525**
- **At 1700**
- **On 22nd October 1996 and thereafter**

Similarly the IV valproate was inappropriate, because there was no confirmation by EEG of the diagnosis. I should mention that a drop in sodium level and cerebral oedema may themselves provoke seizures and I would expect that this possibility would be taken into consideration. For the same reason the giving of midazolam was inappropriate.

(e) Whether Dr Webb should have been aware that sodium metabolism may have been affected by an acute neurological illness of the type experienced by Claire, and if so, how this should have affected his management of Claire.

Dr Webb should be aware of inappropriate ADHD secretion in acute brain illness and the need to monitor sodium levels / conscious level and fluid balance.

(f) The appropriateness of otherwise of Dr Webb's request for the administration of an intravenous dose of sodium valproate.

Answered above.

(g) **At the time of Dr Webb's last assessment on the ward (1715hrs), a nursing note referred to Claire being given a stat dose of Epilim and describes Claire as "Very unresponsive – only to pain. Remains pale. Occasional episode of teeth clenching ..." If that was an accurate description of Claire's state at that time, whether Dr Webb should have taken any other action and if so what.**

This state required a diagnostic assessment of the cause of her deterioration including electrolytes, EEG and head scan. I would have expected the differential diagnosis to include the items on the list given above and specifically this should have included the causes of raised intracranial pressure in this setting since they are quite common and potentially treatable.

(h) **Whether Dr. Webb should have gone over Claire's clinical notes and the drug prescription at Ref: 090-026-075 as part of his Review.**

Review by Dr Webb should have included a review of the prescribed drugs though this may not be in a written account.

(i) **Had Dr. Webb known that Claire had been administered: (a) 635mg of Phenytoin, and (b) 120mg of Midazalam given 'IV Stat', how should that have affected his review and assessment of her condition.**

I am still doubtful if 120mg midazolam was given but if it had it would have been an indication for urgent transfer to ITU and being prepared to ventilate.

(vi) **The appropriateness of the procedure for the alleged transfer (according to Dr Steen Ref: 091-011-067) of Claire's care from Dr Steen to Dr Webb, including:**

(a) **The circumstances in which a transfer of care takes place, how it should have been done and whether the transfer should be recorded in the case notes.**

(b) **How the transfer of care between consultants is normally communicated to the medical and nursing team.**

Neurological involvement in a child's management is differently managed in different hospitals / units. The neurologist may give an opinion but the management is left with the paediatric consultant, or the paediatric neurologist may take over care. Both are appropriate models of care, providing it is clear to everyone who has consultant responsibility. The hospital notes should make it clear if there has been a transfer of care. My reading of Dr Webb's note on page 66 of the notes is that he is making suggestions and not taking over care, but I can't be sure about this. If care is transferred a note is made in the hospital notes and somebody, consultant or registrar tells the nursing staff.

(c) **Whom you would have reasonably expected to have been responsible for Claire's care after 1700 on 22nd October (when Dr Webb makes his last note)**

(d) **To whom you would have reasonably expected that individual to be accountable.**

(e) **When a child is referred from the admitting paediatrician to a neurologist, how both of their teams know who has continuing responsibility and whether this was clear in this case.**

It appears to me that Dr Webb was giving advice to the paediatrician and although as a paediatric neurologist this advice would carry a lot of weight, the final responsibility remained with the paediatrician – at least that is my reading of the notes.

(f) Whether the omission of any evidence in the medical notes that on 22nd October 1996 Dr Webb communicated his opinions and/or advice to Dr Steen is of any concern.

I think it is normal practice for a consultant to give an opinion in the hospital notes with a member of the consultant paediatrician's team, registrar or house officer present and for the latter to communicate with their consultant.

(vii) The quality of the diagnostic assessment and management by the on-call paediatric SHO (possibly Dr Neil Stewart) and the registrar Dr Brigette Bartholome, including:

(a) The SHO's reaction when he was informed that Claire was showing further seizure activity at 2100h on 22nd October 1996, and what action should have been taken at the time, given Claire's overall condition.

The seizure at 21.00 on 22nd October 1996 may not have prompted any further action by the SHO, but the drop in the GCS score should have prompted contact with the Registrar and / or Consultant.

(b) Your comments on Dr Stewart's note following the blood sample taken about 2130, noted at 2330h as having a serum sodium of 121mmol/L, in which he noted his conclusions about this, the action he considered taking and the advice he received from his registrar, Dr Brigitte Bartholome.

On receipt of the serum sodium concentration result at 23.30 on 22nd October, I would have expected both action and a neurological examination. Dr Stewart's assessment of the significance of a low sodium / fluid overload was appropriate at SHO level. However I would have expected the registrar / consultant to have acted on the assumption of cerebral oedema by restricting fluid intake to 2/3 of normal requirements to avoid further water overload which might contribute to cerebral oedema by inducing a diuresis (by Mannitol or furosemide/frusemide) and ventilating her to reduce her partial pressure of carbon dioxide (PCO_2) to reduce intracranial pressure. Following the line of management of non-convulsive status was inappropriate.

(c) Whether either the SHO or registrar should have been informed either Dr Steen or Dr Webb of these events, and if so, whom they should have informed.

Certainly the consultant should have been informed.

(d) Whether you consider that any actions could or should have been undertaken at 2100h or at 2330h that would have prevented Claire's sudden collapse at 0230h. If not, please comment on whether the paediatric team on duty from 1700h should have been able to predict the possibility of a potentially brain-damaging condition and, if so, what action was available for prevention.

It is difficult to know if she would have been retrievable by the measures outlined above but it is quite possible. From my perspective the electrolytes should have been repeated much earlier and a scan performed and seems likely to have shown a low Na level and brain oedema, which could have been treated. Claire was certainly retrievable early-mid 22nd October 1996; thereafter it is more difficult to say.

(viii) The quality of the neurological observation chart recordings, in particular the estimates, initiation and frequency of GCS observations, including whether any particular recorded measurement or measurements should have provoked medical review and, if so, what action was required.

Claire's reduced conscious level ought to have prompted medical action. GCS/CNS observations ought to have been commenced from the ward round. It seems that there were sufficient observations to prompt medical action on the basis of a deteriorating situation given the findings on the ward round early on 22nd October e.g. "pupils sluggish to light" (Ref: 090-022-053) but the team were firmly sticking to non-convulsive status as the diagnosis which seems to have stopped other avenues being pursued until it was too late.

(ix) Whether at any stage, a CT scan should have been sought, and if so, when, by whom, why and what effect this might have had on Claire's diagnosis and treatment.

An early CT/MRI was indicated to provide evidence of intracranial pathology that would account for the deteriorating neurological state and help to decide if there was any suitable treatment. In this case cerebral oedema could have been identified earlier and treated as outlined above. Other conditions that might have been identified are inflammatory diseases e.g., encephalitis.

(x) The appropriateness of the decision to admit Claire to PICU at 0315h on 23rd October 1996, and if so:

(a) At what stage she should have been transferred.

Admission to PICU was appropriate. It should have been earlier if the cerebral oedema had been identified and elective rather than emergency ventilation instituted. Elective ventilation can be used for neurological reasons to reduce raised intracranial pressure – this would require admission to PICU. Admission to PICU need not only be where a patient is unable to breathe him/herself. Cerebral oedema is a critical illness and an indication for ventilation. I would expect this to be done with reduced consciousness and a low sodium level if fluid restriction and inducing a diuresis was not effective in improving the child's condition. Thus this would I think have been considered early on 22nd if the repeat electrolytes and CT had been performed.

Lowering the PCO_2 by hyperventilation is a potent method of reducing intracranial pressure. It works mainly by vasoconstriction and involves reducing the PCo_2 from its normal levels of about 35 to 45/50 mmHg to 25-30 mmHg. The patient may be maintaining reasonable blood gases but the indication for intubation and ventilation and thus admission to Intensive Care is based upon their neurological disease not respiratory failure.

(b) What factors should have led to the conclusion to transfer to PICU.

Deteriorating conscious level and the need for elective ventilation and other treatment for cerebral oedema.

(c) On whom should the responsibility lie of deciding whether admission to PICU was appropriate.

It is a joint decision between the consultants concerned. (i.e. Dr Steen and Dr Webb).

(d) **The effect that admitting Claire to PICU at an earlier stage would have had on her diagnosis and treatment.**

The outcome might have been better but only if the diagnosis was made and treatment urgently instituted.

(xi) **When Claire was admitted to ICU at about 0315h on 23rd October 1996 when she came under the care of Dr McKaigue (anaesthetist) but it is clear that Dr Steen attended the ward and made at note at 0400 on 23rd October 1996. Dr Steen also contacted Dr Webb who attended and made a note at 0440h. What do you consider to have been Dr Steen's clinical role from the time of admission to ICU and that of the first brain stem death tests?**

As I understand it, prime clinical care in PICU was with Dr McKaigue. It would be normal practice for the referring paediatrician to maintain contact. However my reading of the notes suggests that the respiratory arrest was the terminal event and that there was no likelihood of recovery after this and the admission to PICU.

(xii) **Whether given the information that was available to Dr Steen before the post-mortem examination, the stated cause of death on the death certificate was reasonable and / or appropriate. In particular, whether hyponatraemia should have been entered on the death certificate.**

I think it was appropriate to include hyponatraemia on the death certificate as it was the main cause of cerebral oedema which was the main cause of death.

(xiii) **The communication by medical staff with colleagues and with Claire's family, including:**

(a) **The accuracy and appropriateness of the explanation given by Drs Steen and Webb to Claire's parents for why Claire's brain had swollen, as per the "Relatives Counselling Record" (i.e. that it was probably caused by a virus), including other possibilities that should have been raised.**

The information given to the family was in line with the medical view of the illness which had not included a major consideration of cerebral oedema / hyponatraemia until after the CT scan when the information should have been included. Thus although a virus may have been the initiating cause, cerebral oedema caused or aggravated by hyponatraemia was the ultimate cause of death and should in my opinion have been stated.

I would have expected Claire's parents to have been informed on 22nd / 23rd October of the serum sodium concentration results on 22nd and 23rd October 1996; hyponatraemia; SIADH; suspected Encephalitis/Encephalopathy and suspected Non-convulsive Status Epilepticus – as these were the diagnoses being considered. I would have expected Dr. Webb to have asked the medical team if they would like him to speak to the parents and to have invited a member of that team to join him. The medical team could have chosen to speak to the parents themselves or could have asked Dr. Webb to do so with a SHO. Claire's parents should have been kept informed of the situation before they left at about 21.30 on 22nd October, provided that the nurses noticed or were aware that they were leaving. Very often parents would ask about their child's condition before leaving.

(b) The accuracy of Dr Steen stating that Claire's parents should have been spoken with before they left the hospital at about 2130h on 21st October 1996, including who should have spoken to them and what information should have been conveyed.

I am not sure that I can comment on this.

(xiv) Whether you would have expected Claire's death to have been reported to the Coroner at the time, and if so, why and by whom.

I would have expected a full post mortem as the death was unexplained.

I would have expected the death to be reported to the coroner because of the cause of Claire's long term problems is not known, the cause of the acute illness is not known and the cerebral oedema needs explanation. Thus, the consultant caring for her at the end would inform the coroner.

If the RBHSC had decided not to report the death to the Coroner, it was in the parents' hands what type of post mortem should be done, if any. A limited brain only post mortem was an attempt to obtain a clue as to diagnosis including status epilepticus and the cause of death. I do not understand how the hospital could be sufficiently clear about the cause of Claire's death so as not to require it to be reported to the Coroner. However since that was the view it was reasonable to obtain information from a brain only post mortem to 'obtain a clue' as to the diagnosis and cause of death.

(xv) Please [...] the comments of Dr Dewi Evans, consultant paediatrician at Singleton Hospital. Please confirm if this topic is within your expertise, and, if so, please comment on Dr Evans' hypothesis with regard to the blood / CSF white cell ratio.

I am not sure how reliable post-mortem CSF cell counts are. There was not a gross excess of white cells and the post mortem did not show evidence of meningo-encephalitis. Thus I do not regard this as a well-supported conclusion.

(xvi) The treating doctors at the time, the pathologist who conducted the post-mortem, the Experts called by the Coroner and the Experts who made statements to the PSNI have all given different interpretations of the likely nature and course of Claire's illness. From your perspective as a paediatric neurologist, can you equate these opinions such that you can offer a rational explanation for the course of events and the cause of the cerebral oedema? Please describe any remaining uncertainties.

My reconciliation of information available is that this patient had long standing, unexplained cognitive impairment and an unexplained acute encephalopathy with terminal cerebral oedema with hyponatraemia related to inappropriate ADH secretion. The latter sequence is not uncommon in a range of acute brain illness and requires urgent identification and management otherwise it may be fatal.

As to the nature of the encephalopathy the working diagnosis was subclinical epilepsy in which although I think is unlikely an EEG would have demonstrated if this was the case. If it was it would have been normal practice to consider giving an anaesthetic agent e.g., propofol or thiopentone as more powerful anti-epilepsy drugs with ventilation rather than giving a number of anti-epilepsy drugs which had the capacity to sedate. This however does not remove the necessity to diagnose and manage the inappropriate ADH secretion. However these anaesthetic agents can have serious side effects and the question of whether to treat this condition if it existed or observe would be discussed.

(a) What might have been the antecedent cause of SIADH in Claire's case?

The cause of Claire's SIADH is not known e.g. it may have been a metabolic problem or bacterial infection. The immediate antecedent cause might have been a virus infection involving the brain. I do not know of evidence that her long term brain impairment would predispose her to inappropriate ADH secretion.

Any child with a neurology problem is more likely to develop significant SIADH. This ought to have been factored into her fluid management by prescribing less fluid and administering a fluid with a higher sodium content, both pending the electrolyte results on 21st October and also on receipt of those results. The problem was the failure to repeat the sodium test 6 hours after the first blood sample was taken.

The chest X-ray showed a clear abnormality. Pneumonia could be part of the intercurrent viral illness. It could be related to SIADH. It is possible that Claire had pneumonia. It would be worth getting an opinion on whether the chest X-ray shows primary lung infection or infection secondary to inhalation.

(b) State at what time and on what date the clinicians ought to have been aware of the risk of SIADH in Claire.

The possibility of developing SIADH should have been raised when the first plasma Na was returned as 132 mmol/l. It should have been seriously considered during 22nd October day time when she had become more drowsy, vacant and showing little response.

(c) Do you agree with the Coroner's finding of the three causes of cerebral oedema, namely: (a) SIADH, (b) hyponatraemia, and (c) status epilepticus?

SIADH and hyponatraemia are fair. I do not see evidence for status epilepticus.

(d) Do you regard status epilepticus as having been a contributory cause of Claire's death?

There is no clear evidence of status epilepticus and I cannot understand why an early EEG was not performed. I do not agree that it was a contributory cause of death. The history recorded by Dr. Webb at 17.00 on 22nd October 1996 from Mrs. Roberts of *"She had some focal szs on Monday and Rt sided stiffening"* is evidence only of convulsive epilepsy, not non-convulsive status epilepticus. A diagnosis of non-convulsive status epilepticus can only be made by EEG.

(e) State whether you agree that Claire may have required fluid restriction on the basis, expressed by Dr Bingham at the Inquest, that she would have had *"a low level of metabolism due to reduced consciousness."*

I think the more compelling reason was the low sodium level but reduced consciousness is also a factor.

(xvii) State how long a post-ictal state would normally be expected to last

(a) In a 9 year old child generally and

(b) In Claire's case

There is wide variation from a few seconds to more than 1 hour and there is no evidence available about Claire's situation.

(xviii) State whether the infusion of midazolam could affect the Glasgow coma scale:

(a) Generally and also

(b) In Claire's case, and if so, state how and the reasons why

Yes, it can reduce the conscious level and thus the GCS because it is a sedative.

(xix) State what level of the Glasgow coma scale would give cause for medical concern in this case.

A drop in GCS would cause concern. Scores of 9-12 require investigation and explanation and less than 9 require urgent investigation and management. This statement applies to Claire's case and is also of general application. The low GCS was unexplained and could signify raised intracranial pressure which might be treatable e.g., cerebral oedema. If a GCS score is of concern, very often the nurse will invite a more senior nurse e.g. ward sister / nurse in charge and / or the SHO to assess the GCS. Any fall in GCS is noteworthy. The GCS trend is important.

(xx) Please provide your opinion on the quantity (12mg) of Midazolam intended to be given 'IV Stat' to Claire, the effect that it would likely have had on Claire and in particular, the extent to which such a dose of Midazolam could have induced anaesthesia in Claire

My reading of this is that 12mg IV stat dose of Midazolam was calculated as 0.5mg/kg and it was given. The Roche sheet for that time recommends 0.03-0.3mgm/kg as a loading dose, so this is an overdose.

The overdose of 12 mg IV stat of midazalam administered at approximately 15.25 (Ref: 090-026-075, 090-040-141) could have caused or contributed to this fall in Claire's GCS. The effect of this drug could have lasted at least 1-2 hours. There was no evidence that Claire needed this dose of medicine. It was a big dose. It likely reduced her conscious level and therefore reduced her breathing and increased her PCO_2. Therefore it was likely to have exacerbated her condition. It is possible that this medicine tipped her over to a higher PCO_2 level which caused greater cerebral oedema. It is also possible that it just added to what was already happening. Most important is the failure to treat Claire's underlying condition which was treatable. The main point is that the clinicians missed what was wrong with her and had slender reasons for a diagnosis of non-convulsive status epilepticus. The midazolam did not treat her underlying condition or the cerebral oedema.

(a) State whether Midazolam was a controlled drug in October 1996.

Hypnovel (Roche preparation of Midazolam) in the 1999-2000 Compendium of data sheets was recorded as: Legal Status UK:CD(Sch4),POM. Last review July 1996.

(xxi) Please provide your opinion on the effect that a dose of 120mg of Midazolam given 'IV Stat' would have had on Claire and her presentation at that time, and in particular:

(a) The extent to which 120mg of Midazolam could have induced anaesthesia in Claire

(b) The extent to which 120mg of Midazolam would have affected the central nervous system observations and level of consciousness in Claire

(c) Claire's symptoms that would have been attributable to the administration of 120mg of Midazolam from 15.25 onwards

(d) Claire's symptoms that would not have been attributable to that medication

(e) The effect that 120mg of Midazolam would have had on Claire's fluid management, sodium level and SIADH

(f) The effect that 120mg of Midazolam would have had on Claire in combination with the other medications she was receiving

The 120mg dose is very odd. As written at 3.25pm on 22.10.96 as a Drugs–once only prescription (Ref: 090-026-075) by Dr Stevenson it does look like 120mg but is not signed off. This does not look to be the continuous infusion since that is in the regular prescriptions (also Ref: 090-026-075). My reading of the nursing notes (Ref: 090-040-141) is that the 12mg of midazolam was given as a start dose of hypnoval at 3.25pm followed by the continuous infusion of midazolam. If a start dose of midazolam 120mg had been given it would have been a gross overdose likely to produce marked respiratory depression (stopping her breathing) and reducing conscious level, but I do not think it is likely that it was given. It would also have seemed an excessive amount to draw up from hypnoval ampules as a start dose. This requires explanation.

(xxii) Explain:

(a) What a neurological examination ought to have entailed in Claire's case.

(b) How pupil response, eye movements, spontaneous movements of limbs, and tone, power and reflexes in all four limbs would likely be affected by hyponatraemia.

(c) If Claire had hyponatraemia developing during the day on 22nd October 1996 what symptoms would likely have been apparent on neurological examination and why.

(d) The meaning/significance of each of the findings in the neurological examinations carried out on Claire on 21st October on admission, on the ward round, by Dr. Webb at 14.00 and at 04.00 on 23rd October by Dr. Steen.

(e) The symptoms of raised intracranial pressure and its treatment.

The main effect of cerebral oedema is of reducing conscious level and thus of a drop in GCS. The pupil reactions become sluggish and ultimately fixed dilated pupils occur. Breathing may be temporarily increased with mild increased intracranial pressure but with higher pressure breathing is depressed and unless ventilated the subsequent rise in PCo_2 will worsen the cerebral oedema. Sedative drugs will tend to reduce both conscious level and breathing.

If intracranial pressure rises rapidly the signs of "coning" may appear. These start with upward eye movements followed by extensor spasms of the trunk and limb stiffening which may be intermittent and may be absent. After prolonged raised intracranial pressure the limbs may be flaccid but the neurological signs may be modified by drug treatment. The pressure changes may take several days to be obvious in examining the fundi. In Claire's case the ventilation should in my view have been performed earlier, for the above reasons.

The examinations performed would consist of pupil reactions, GCS, pulse, BP, breathing rate and PCo_2 and o_2 and tone in the muscles of the trunk and limbs and tendon reflexes. In her case there was little evidence of coning and the GCS and pupils were the main evidence.

The fluid requirements of Claire would normally have been 65ml/kg (24.1) / 24 hours, which makes a total of just over 1500ml. My recommendation would have been to give two thirds of this total, i.e., approximately 1000ml /24 hrs.

- *"Claire was admitted to the Royal later on 21st October 1996 exactly 4 months after the conclusion of the Inquest into Adam Strain's death of hyponatraemia at the Royal. The A&E note repeated parts of that history and noted non-bilious vomiting 'since this evening'. She was 'drowsy, tired, apyrexial' with no other abnormal signs except for increased left sided muscle tone and reflexes. At 2045, a decision was made to admit Claire to hospital under the care of Dr. Heather Steen."* (Ref: Your brief 18)

Drowsy, tired, apyrexial and vomiting with increased left sided muscle tone and reflexes. These findings would be compatible with any cause of a brain illness with vomiting as a possible sign of raised intracranial pressure. The motor signs, if new, would be compatible with such an illness.

- *"The admission note (timed at 2000) refers to Claire as 'vomiting at 3 pm and every hour since' and to her having experienced a loose bowel motion 3 days previously. The admitting doctor, Dr. O'Hare, noted that Claire had severe learning difficulties but normally had meaningful speech and referred to the recent trial of Ritalin and its apparent side effects[1]. Dr O'Hare also noted that Claire 'sits-up and stares vacantly' and was ataxic. She was not responding to her parents' voice and only intermittently responding to a deep pain stimulus. She had cogwheel rigidity of her right arm and increased tone in all other limbs. Tendon reflexes were brisker on the right than the left and there was bilateral ankle clonus. "* (Ref: Your brief 19)

"Sits up and stares vacantly and was ataxic". "Responding to the parents voice and only intermittently responding to deep pain stimulus. She had ankle clonus.

This indicates a brain illness with reduced consciousness which may have been of fluctuating severity eg, apparently responding to parents but not to deep pain. The motor signs had shifted from L (in 18) to more obvious on the R in 19. These again suggest fluctuation and deterioration. 18 and 19 would make a rise in intracranial pressure a high priority and would be compatible with hyponatraemia.

- *"At 1530 Claire was reported as having a 5-minute 'strong seizure [sic]' at 1525. At 1630, her teeth tightened slightly. At 1600, Dr. Webb made a note. He saw Claire with her grandmother, noting a history of 'Vomiting and listless yesterday p.m. – followed by prolonged period of poor responsiveness.' He added that she had appeared to improve after rectal diazepam, given at 1230. She was afebrile and pale with no meningism. She opened her eyes to voice, was non-verbal, withdrew [limb] from painful stimulus and had (questionably) reduced movements on the right side. He found mildly increased tone in her arms and symmetrical brisk reflexes, sustained ankle clonus and upgoing plantar responses. Claire was sitting up with eyes open and looking vacant, not obeying commands. She did not have papilloedema[2]. Dr Webb's impression was 'I don't have a clear picture of prodrome + yesterday's episodes. Her motor findings today are probably long-*

[1] Ref: 090-022-050
[2] Ref: 090-022-053, 054

standing but this needs to be checked with notes. The picture is of acute encephalopathy, most probably postictal in nature.." (Ref: Your brief 29)

The responsiveness data were improved upon those noted above in 19 but remained non-verbal. The motor signs again were somewhat different from those above and again suggested fluctuation. These were again compatible with raised but fluctuating intracranial pressure. The lack of papilloedema would not exclude this since it can take 1-2 days for this change. The fluctuation in the motor signs should have been taken as most likely to indicate such a process and require urgent CT / MRI scanning.

- *"At 1700 Date, Dr Webb, having received information from Claire's mother about the onset of the illness, described Claire as 'largely unresponsive' with intermittent vomiting and chewing. He prescribed the antibiotic cefotaxime and the anti-viral drug acyclovir for 48 hours, although he noted that he did not think meningoencephalitis very likely. He noted that stool, urine, blood and a throat swab should be checked for evidence of enterovirus infection. He also suggested an additional anticonvulsant intravenous infusion: sodium valproate 20 mg/kg as an initial dose, followed by 10 mg/kg over 12 h. A nursing note at 1715 referred to Claire being given a stat dose of Epilim and added 'Very unresponsive – only to pain. Remains pale. Occasional episode of teeth clenching ..." (Ref:* Your brief 34)

In the above the clinical signs noted refer to lack of responsiveness which indicates a continuing significant level of coma and that the treatment given had not been associated with improvements.

- *"Claire was admitted to ICU at 0315 on 23rd October 1996 and the first ICU note was made at 0400. It reiterated the history as given above and noted that 'Claire was 'now intubated and ventilated. Pupils fixed and dilated. Bilateral papilloedema [swelling of the optic discs visible using an ophthalmoscope and implying raised intracranial pressure] L>R. No response to painful stimuli ...' She was given mannitol to reduce the cerebral oedema and dopamine and a brain CT scan was requested. At that time, the serum sodium concentration was recorded at 121mmol/L, which was equivalent to the result recorded at 2330 on 22nd October 1996. It is not clear precisely when those bloods were taken or the laboratory results communicated but the phenytoin result states that it was received at 0420 and vetted at 0438. The blood could therefore have been taken between 0315 and 0400."* (Ref: Your brief 42)

The appearance of papilloedema indicates severe raised intracranial pressure and the pupil signs and lack of responsiveness suggest widespread severe brain damage as would be anticipated from uncontrolled cerebral oedema, preventing sufficient blood to reach the brain. The sodium levels of 121 mmol/L is sufficient cause of this problem. Mannitol, an osmotic diuretic was given and this was appropriate to attempt to reduce the water content of the brain but was in my opinion given much too late and sadly was not effective.

(xxiii) Please comment on:

(a) Whether it was reasonable or appropriate for Dr. Webb to have formed the view that Claire's "motor findings today are probably long standing but this needs to be checked with notes":

This was a reasonable question to ask but the fluctuation discussed above indicates that there was an active process occurring whether or not

- **having only spoken to Claire's grandmother, and not her parents, at about 14.00.**

  I cannot comment in detail but if her grandmother knew her well she could helpfully comment on whether Claire had a motor disorder.

- **given Claire's history of previous epilepsy which was in remission on admission.**

  This was not relevant in my view.

(b) Whether you would have expected the Coroner to have been informed of the intention to perform a limited post mortem before proceeding with it and if so why.

I don't know the normal practices of this coroner but if the death was not referred, I think there would be no obligation to inform the coroner

Statement of Truth

I understand that my duty as an expert is to provide evidence for the benefit of the Inquiry and not for any individual party or parties, on the matters within my expertise. I believe that I have complied with that duty and confirm that I will continue to do so.

I confirm that I have made clear which facts and matters referred to in my report(s) are within my own knowledge and which are not. Those that are within my own knowledge I confirm to be true. The opinions I have expressed represent my true and complete professional opinions on the matters to which I refer, having studied all the relevant documents supplied to me.

I confirm that I have no conflict of interest of any kind, other than any disclosed in my report(s). I do not consider that any interest that I have disclosed affects my suitability as an expert witness on any issue on which I have given evidence. I undertake to advise the Inquiry if there is any change in circumstances that affects the above. I have no personal interest in supporting any particular point of view.

I understand that I may be called to give evidence.

Signed:  Date: 24.5.12.

Professor Brian Neville