Supplementary Report on

Claire Margaret Roberts (deceased)

Date of birth: 10 January 1987

Date of death 23 October 1996

Supplementary report on:	Claire Margaret Roberts (d.o.b. 10.01.1987)
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Instructed by:	Ms B Conlon Administrator Inquiry into Hyponatraemia-Related Deaths (IHRD)
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Instructions

In my original report (March 2011) I stated as one of my conclusions:
"*It would be helpful to gain an understanding from Dr Harding as to whether, in his experience, an acute and fulminant encephalitis causing cerebral oedema, coning and death in the space of three days could occur in the absence of clear neuropathological changes, possibly as a result of the rapidity of development of such an infection.*"

In addition to the documentation listed in my March 2011 report I have now received in addition
- a briefing paper furnished to Professor Brian Harding;
- a brief supplementary report from Prof Harding addressing my query as set out above.

I am now instructed to consider Prof Harding's supplementary report (dated 24 March 2011) and to make any further comments that I feel are necessary.

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

I confirm that I have no conflict of interest of any kind, other than any disclosed in this report. 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 Secretariat if there is any change in circumstances that affects the above.

K.A.V. Cartwright
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Prof. KAV Cartwright

Summary of my previous conclusions

1. It is outwith my expertise to assess whether or not hyponatraemia caused or contributed to the cerebral oedema that led to coning and to Claire's death though I observe that inappropriate ADH secretion is a well-recognised complication of both meningitis and encephalitis.
2. Claire did not die from (or with) meningitis, either viral or bacterial.
3. In my view her clinical presentation, the progression of her illness and results of tests on blood and CSF were consistent with an acute and fulminant encephalitis.
4. However, Dr Harding, consultant neuropathologist, found no neuropathological evidence to support such a diagnosis.
5. It would be helpful to gain an understanding from Dr Harding as to whether, in his experience, an acute and fulminant encephalitis causing cerebral oedema, coning and death in the space of three days could occur in the absence of clear neuropathological changes, possibly as a result of the rapidity of development of such an infection.

My further conclusion having read Prof Harding's supplementary comments

1. Though I am unable to account for the absence of neuropathological evidence of encephalitis, a viral encephalitis remains in my opinion the most likely cause of Claire's death.

Opinion

Preamble

In my original instructions I was asked to explore the issue of the difference of opinion between Dr Dewi Evans, Consultant Paediatrician, and Dr (now Prof) Brian Harding, Consultant Neuropathologist, regarding the underlying cause of Claire Roberts' death. Dr Evans thought that an intracerebral infection was the most likely cause.

In contrast, Prof Harding excluded an infectious cause on the basis of the lack of any neuropathological evidence to support such an explanation. In his opinion hyponatremia was the most likely cause of Claire's death because other causes had been excluded.

In my original report I set out the microbiological evidence that led me to support Dr Evans' view (that there was strong evidence of an acute infection with intracranial involvement in the period immediately prior to Claire's death).

If Prof Harding's further opinion had been that an infectious aetiology could be possible if it had been so rapid that there had been no time for definitive neuropathological changes to have occurred, then in my opinion this would have reconciled the apparent difference of opinion between the two experts.

However, Prof Harding's further opinion is that "*Given the marked degree of brain swelling noted clinically (including papilloedema and CT scan) and confirmed at post-mortem, I consider it extremely unlikely that microscopic evidence of encephalitis would not be evident by 3 days. I have seen it occurring within 36 hours.*".

The current position with regard to the opinions of these two experts thus remains as before – Dr Evans considers and infectious aetiology the most likely explanation for Claire's death, whereas Prof Harding excludes such a possibility and as a consequence considers that hyponatremia was the most likely explanation by a process of elimination of other possibilities.

A recapitulation of the evidence supporting an infection as the cause for Claire's admission to hospital on 21 October 1996

1. When Claire was referred to the Royal Belfast Hospital for Sick Children on 21 October 1996, there was a short history of an acute illness with lethargy, vomiting, slurring and then wiithdrawal of speech. This was superimposed on a long background history of seizures and moderate developmental delay, but definitely appeared to be a new, acute episode and with changing neurological features. Not surprisingly, on admission to a paediatric ward, the differential diagnosis included viral illness and encephalitis.

2. In addition to hyponatremia, blood tests also revealed a raised total white blood cell count of 16.5 x 10^9/L, well above the upper limit of normal, and for which by far the most likely explanation was an acute infection of some sort. Regrettably, no differential white blood cell count was done, or if it was, the results have now been lost. A differential white blood cell count on a total count of 16.5 x 10^9/L would have been likely to have differentiated between viral and bacterial infection with a high degree of reliability.

3. Claire suffered seizures and then at 2.30 am on 23 October a respiratory arrest. The arrest was almost certainly caused by coning secondary to cerebral oedema and raised intracranial pressure. Both the seizures and the respiratory arrest could have been caused by an encephalopathy of infective or non-infective origin.

4. CSF obtained at autopsy on 24 October 1996, the day after Claire's death, showed an extremely high (and unexplained) protein level, a red blood cell count of 300,000 per mm^3, and a white blood cell count of 4,000 cells per mm^3, with most of the white blood cells being mononuclears i.e. lymphocytes. If the red blood cells in the CSF specimen had reflected solely contamination of CSF with peripheral blood (i.e. an artefact associated with the collection of the specimen) then if the peripheral white blood cell count was around 5.5 x 10^9/L (as it was on 24 October 1996) it would be expected that a red blood cell count of 300,000 per mm^3 would be accompanied by around 300 white blood cells.

5. If the peripheral white blood cell count had comprised the expected proportions of neutrophils and lymphocytes, then the predominant white blood cells in the CSF would have been neutrophils. In fact, the cytology studies of the autopsy CSF showed (a) a total white blood cell count that was more than tenfold higher than would have been explained by the numbers of red cells present and (b) the majority of those cells were lymphocytes, whereas even in viral infections, lymphocytes rarely predominate to any great extent in differential peripheral white blood counts when these are obtained early in the illness.

6. The most likely explanation of these CSF findings is that there was an acute infective or inflammatory process at work in the CSF at the time of Claire's death. The fact that the white blood cells were predominantly lymphocytes made it most likely that a virus and not a bacterium was the cause.

7. An alternative but much less likely possibility is that the red and white blood cells in the CSF sample were indeed due to blood contamination, but if so, the blood contained a substantial relative excess of white blood cells, of which the majority were lymphocytes. The most likely explanation for such gross lymphocytopenia would have been a systemic viral infection.

8. In either case, the likelihood that Claire had a viral infection at the time of her death is high. The cytological evidence from the CSF suggests strongly that such viral infection was present intracerebrally as well as systemically, and was consistent with Claire's clinical presentation. The alternative hypothesis that Claire's death was due to hyponatremia does not explain (a) the fact that she became unwell prior to her admission to hospital with what appeared to be an acute infection, (b) her markedly high peripheral white blood cell count on admission, or (c) the relative leucocytosis and lymphocytosis in Claire's CSF.

9. Though I am unable to account for the absence of neuropathological evidence of encephalitis, this remains in my opinion the most likely cause of Claire's death.