Adam STRAIN

DOB: 14th August 1991

Comments on the reports by Prof Rating

Prepared by Dr Fenella Kirkham MB BChir FRCPCH

Professor of Paediatric Neurology

Institute of Child Health, London

&

Consultant Paediatric Neurologist

Southampton General Hospital

Prepared under the instruction of the Hyponatraemia Inquiry

In his reports, Prof Rating states that he believes that the only cause of Adam's death was too much free water given too rapidly before 0932 on 26th November 1995. Using his calculations of brain, blood and CSF volumes, which I do not dispute, although I note that there is 'fuzziness' as well as extrapolation from adults to children, he considers that this alone led to sufficient cerebral oedema to cause intracranial hypertension leading to cerebral herniation. I do not think that there is evidence from previously reported literature or our joint clinical experience or Adam's case to support this thesis of sole causation of cerebral oedema and brain death by dilutional hyponatraemia. My ongoing clinical experience and the available literature suggests that cerebral herniation through the tentorium cerebelli and/or the foramen magnum typically occurs when there are differences in pressure between compartments. I do not disagree, and neither does Dr Squier, that Adam is likely to have had intracranial hypertension. However I do not think that the available evidence suggests that this was simply due to osmotic cell swelling at a rate faster than the cells' ability to pump sodium out. As Prof Rating acknowledges, in addition to focal mass lesions, acute intracranial hypertension may occur in venous sinus thrombosis or when 'an increase in cerebral perfusion pressure eventually becomes counter-productive because of the associated increase in intracranial pressure' as in hypertensive encephalopathy/posterior reversible encephalopathy syndrome (Griswold et al 2012).

In view of my longstanding interest in causes and consequences of coma, I am aware of the literature on encephalopathies secondary to electrolyte disturbances, including the association of hyponatraemia with myelinolysis as well as cerebral oedema, and have used this knowledge when writing reviews. From Dr Squier's report and my understanding of the time course of myelinolysis from my clinical experience, I do not think that we can diagnose or exclude myelinolysis in Adam's case, but the striking finding is brain death in the context of cerebral oedema particularly involving the posterior fossa. I note that at the time of his second report, Prof Rating had access to both my reports but I am not sure that he had seen my excel spreadsheet documenting the clinical findings in all the published cases of hyponatraemic encephalopathy that I could find on a search of Pubmed and a hand search of all the references from the initial papers, i.e. as unbiased an approach as possible. I found the review by Samuels and Seifter useful although the statements on hyponatraemia were not referenced and I do not think that there are any new data not already part of the overviews by Arieff, Ayus and Moritz or my excel spreadsheet. As documented in many cases, including those tabulated in my excel spreadsheet and in Prof Rating's very useful description of his experience from Berlin, seizures are common in acutely hyponatraemic children, particularly if there are risk factors for hypoxia, e.g. bronchiolitis (see paragraph 54 of my report of 30.3.2012). However, there is ongoing controversy over whether hyponatraemia alone, however rapid, causes sufficient cerebral oedema to lead to acute intracranial hypertension enough to cause cerebral herniation and brain death. Prof Rating quotes the paper by Witt which found no evidence for acute cerebral oedema or intracranial hypertension in piglets rapidly infused with hypotonic solutions. I was not able to find a single convincing clinical case and I note that Arieff and Ayus continue to emphasise the importance of co-morbidities, particularly hypoxia, in their work. Taking this into account, but in view of the normal oxygenation intra-operatively in Adam's case, Prof Rating hypothesises that osmotic swelling caused hypoxia but he provides only a 1953 reference for this opinion. I included in my report of 30.3.2012 (paragraph 84) the possibility that the acute anaemia increased the risk of tissue hypoxia although there is no histological evidence in Adam's case.

Prof Rating cites the intra- and post-operative low sodiums and the haematocrit of 18% as evidence of dilutional hyponatraemia. I would be grateful if he could clarify the following points:

1. Did the Berlin cases die with neurological signs consistent with intracranial hypertension and brain death?

2. Does Prof Rating think that the haematocrit of 18% was due solely to the excess of free water? The operation was complex and there was considerable blood loss

3. Given that it is now agreed that the hypertension during the second half of the operation was iatrogenic in order to optimise perfusion of an adult-sized transplant kidney, does Prof Rating think that there is clinical evidence of raised intracranial pressure between 0932 and the discovery of fixed dilated pupils at the end of the operation?

4. Can Prof Rating find cases reported in the literature of isolated acute hyponatraemia with documented intracranial hypertension and/or brain death?

5. Can Prof Rating provide evidence that a rapid decline in sodium actually does (rather than ***may***) overwhelm the adaptive mechanisms (240-004-011) to cause cerebral oedema leading to intracranial hypertension leading to cerebral herniation leading to brain death as well as myelinolysis

6. Can Prof Rating provide evidence that retinal haemorrhages occur in cerebral oedema secondary to hyponatraemia (240-004-023) when they are very rare in intracranial hypertension in children (Shiau 2012)

As a minor point, I did take account of Dr Coulthard's opinion on poor feeding in children with chronic renal failure (see paragraph 63 of my report of 30.3.2012). I think that Prof Rating and I would agree that it would be easier to be sure about Adam's pre-operative developmental status if we had access to all the reports, several of which are missing or blacked out in the material to which we have access.

Fenella Kirkham MD FRCPCH

Professor in Paediatric Neurology

Consultant Paediatric Neurologist

21st Dec 2012

Shiau T, Levin AV. Retinal Hemorrhages in Children: The Role of Intracranial Pressure. Arch Pediatr Adolesc Med. 2012 Mar 5. [Epub ahead of print]

Griswold WR, Viney J, Mendoza SA, James HE. Intracranial pressure monitoring in severe hypertensive encephalopathy. Crit Care Med. 1981 Aug;9(8):573-6.